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DIAGNOSIS AND TREATMENT OF LARYNGOTRACHEITIS IN CHILDREN

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monograph

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In this edition, within the framework of the program on otorhinolaryngology, information related to one of the sections - clinical otorhinolaryngology and immunology is summarized. The manual includes not only basic knowledge concerning this subject, but also contains modern scientific knowledge in some of its sections. The monograph is supposed to be used as an auxiliary source of information when conducting practical classes and lectures on the course of otorhinolaryngology for doctors and students.

The monograph presents modern approaches to the diagnosis and prevention, as well as the treatment of acute stenosing laryngotracheitis in children. An algorithm for examining children at risk is presented,

The authors hope that the book will be of some interest to doctors of related specialties - otorhinolaryngologists, allergists, neonatologists, pediatricians, as well as residents, and can be used in the structure of the work of medical and polyclinic healthcare institutions.

Content

Quick reference of terms and conditional abbreviations

AOP - antioxidant protection
URT - upper respiratory tract
DC - diene conjugate
CT - catalase
LII - leukocyte index
MDA - malondialdehyde
ASLT - acute stenosing laryngotracheitis
FLOOR - lipid peroxidation
PSLT - primary stenosing laryngotracheitis
RSLT - recurrent stenosing laryngotracheitis
NSR - medium molecular peptide
SOD - superoxide dismutase
TT - traditional therapy
TF - transferrin
FAN - phagocytic activity of neutrophils
FRIS - immune system disorders formula
HL - chemiluminescence
CIC - circulating immunocomplexes
EI - endogenous intoxication
IL - interleukin
INF - γ - interferon
TNF-α - tumor necrosis factor

INTRODUCTION

According to the World Health Organization, in recent years there has been an increase in the incidence of acute respiratory viral infection. In this regard, the attention of pediatricians and otolaryngologists is attracted by acute stenosing - laryngotracheitis (ASLT). According to the data of many years of research, the number of patients with ASLT ranges from 0.1 to 0.4% of all children hospitalized with a diagnosis of acute respiratory viral infection. The development of stenosing laryngotracheitis in acute respiratory viral infection (ARVI) dramatically aggravates the condition of sick children, and sometimes the life of a child depends on its attachment to the underlying disease.

Since the first days of independence , large-scale reforms have been consistently implemented in our country in order to improve the quality of medical care for the population . Thus, effective medical care for children ensured timely detection, early diagnosis and treatment of patients with ASLT, which made it possible to reduce the duration of their treatment in the hospital by 3-4 days.

Despite numerous scientific studies devoted to the study of the patterns of the infectious process in stenosing laryngotracheitis, the role of dysbiocenosis of the mucous membranes of the upper respiratory tract, the process of endogenous intoxication (EI), which develops as a result of illness in children and its relationship with the course of the disease, as well as the state of the system of local and general immunity dictate the need to improve the methods of their correction in the light of modern requirements. At the same time, the causes of recurrence of acute stenosing laryngotracheitis have not been fully determined; an important task is to develop prognostic criteria for assessing the outcomes of OSLT.

Given the dissertation research to a certain extent serves to solve the problems provided for in the resolutions of the President of the Republic of Uzbekistan No. PP-2133 dated February 19, 2014 “On the State Program“ The Year of a Healthy Child ”and No. PP-2221 dated August 1, 2014 “On the State Program for

Further Strengthening reproductive health of the population, protection of the health of mothers, children and adolescents in Uzbekistan for the period 2014-2018", as well as in other legal documents adopted in this area.

Scientific research aimed at improving the methods of complex diagnostics, treatment and prevention of stenosing laryngotracheitis in children was carried out in many leading medical centers, such as the Schneider Children's Medical Center (Israel), Giessen University Hospital (Germany), St. Mary's Children's Clinic (Germany), Center of Innovative Medicine Interbalkan (Greece), Generale Clinic (Switzerland), Royal Clinic (Great Britain), Queens Medical Center (Great Britain), IDIBAPS Clinic (Spain), St. Luke's Hospital (Japan), Federal Scientific and Clinical Center of Otorhinolaryngology FMBA of Russia (Russia) , as well as the Tashkent Pediatric Medical Institute and the Republican Specialized Scientific and Practical Medical Center for Pediatrics (Uzbekistan).

As a result of the studies, criteria for assessing the risk of occurrence and recurrent course of OSLT were developed, the mechanisms that determine the sensitivity of the respiratory tract were identified (Freiburg Clinic, Germany); established endocrine dysfunction in children with primary and recurrent acute stenosing laryngotracheitis (Children's Hospital, Ireland); the influence of the composition of the microflora of the main loci of the body, connective tissue dysplasia, regulatory systems on the function of external respiration, the formation of threshold sensitivity and reactivity of the respiratory tract in children with recurrent stenosing laryngotracheitis (RSLT) was proved (Melbourne University, Australia).

At present, the goal of many studies in the world is to further determine at the immunomolecular level the role of specific and non-specific factors of immune protection in the pathogenesis of acute stenosing laryngotracheitis; assessment of the state of non-specific protection during OSLT; study of significant changes in the cellular link of immunity, changes in T-suppressors and partially B-lymphocytes; as well as the prevention of relapses and the improvement of methods for diagnosing and treating the disease.

As the analysis of special literature showed, a number of researchers studied the role of the allergic component and the autonomic nervous system in the pathogenesis of the development of primary and recurrent OSLT. According to the results obtained, more than 90% of sick children in the pathogenesis of primary and recurrent acute stenosing laryngotracheitis is dominated by allergic component with the identification of common and allergen-specific IgE . In addition, it has been proven that the development of OSLT in parainfluenza infection is associated with a significant increase in IgE titer and specific IgA in nasopharyngeal secretions in children with ARVI. The mechanisms of OSLT recurrence based on a significant change in the immunological reactivity of the body, which are associated with its allergization by both infectious and non-infectious agents, including adverse environmental, seasonal, meteorological and even social conditions, have been studied. It has been proven that OSLT proceeds with vegetative disorders, which, in turn, have a significant impact on the course and outcome of the underlying disease. An improved treatment of OSLT at the height of the disease is proposed, based on the use of drugs, taking into account the type of initial vegetative tone of the body.

Despite numerous works devoted to the study of acute stenosing laryngotracheitis, its diagnosis and methods of treatment, the trend towards an increase in the recurrence of the disease persists, which dictates the need to study the general patterns of the infectious process in stenosing laryngotracheitis, assess the significance of the microbiocenosis of the mucous membranes of the upper respiratory tract, disorders of the immune and interferon statuses and development of ways to correct them, predict the disease on the basis of a prognostic map, as well as improve the effectiveness of treatment and preventive measures.

CHAPTER I. _ C CURRENT ASPECTS OF THE PROBLEM IMPROVEMENT OF DIAGNOSIS AND TREATMENT METHODS ACUTE STENOSING LARYNGOTRACHEITIS IN CHILDREN (Literature review)

1.1. Acute stenosing laryngotracheitis: predisposing factors , pathogenetic mechanisms of development and its classification

Acute respiratory diseases are the leading pathology of childhood. Their share, together with influenza, is at least 70% in the structure of all morbidity in children. In recent years, there has been an increase in the number of acute respiratory viral infections accompanied by airway obstruction, among which a large proportion is stenosing laryngotracheitis [Alenina T. M., Karavaev V. E., 2002; Arinenko R. Yu., Anikin V. B., Golovkin V. I., 2007 ; Afanasiev O.I., 2006; Blokhin B.M., 2009 ; Bogonosov N.V., 2000; Karpov V.V., Safronenko L.A., Shapranov N.L., 2000; Hogg J. _ C. , 2011].

The prevailing view in the literature is that the cause of ASLT is a viral infection [Alenina T. M., Karavaev V. E., 2002; Arinenko R. Yu., Anikin V. B., Golovkin V. I., 2007; Belousov Yu.B., Karpov M.V., Leonova M.V., Efremenkov O.V., 2006; Zaitseva O.V., 2006; Zaplatnikov A.L., 2004; Krasnov V. V., Anastasiev V. V., Zmachinskaya T. B., 2002; Lukyanov S. V., Sereda E. V., Lukina O. F., Dukhalin A. S., 2003; Martynkin A.S., Ivanova R.A., Dokhalova G.M., Ivanov V.P., Kosenko I.M., 2000; Spiridonova E.A., Lobushkova I.P., 2009; Sukhovetskaya V.F., Sominina A.A., Drinevsky V.P., Milkint K.K., 2004]. It has been proven that this disease can develop against the background of a respiratory disease of any etiology, however, only four types of viruses are of real practical importance: influenza, adenoma virus infection, parainfluenza, pec piracy - syncytial infection [Zaitseva O.V., 2006; Kladova O.V., 2003; Ovsyannikova E.M., 2007; Shaitor V. M., Melnikova I. Yu. , 2007].

T. _ J. _ Fete et al (2006), studying the etiology of ASLT, associated this syndrome only with the parainfluenza virus [Handler S. _ D. , 2005]. Most authors believe that parainfluenza and influenza viruses play the main role here [Kladova O.V., 2003; Ovsyannikova E.M., 2007; Shaitor V. M., Melnikova I. Yu. , 2007 ; Williams J. _ V. , Harris P. _ A. , Tollefson S. _ J. , 2014 ; Pickering , L. _ K. , 2010]. According to S. A. Tsarkova (2001), stenosing laryngotracheitis is more often associated with the parainfluenza virus, which accounts for 33-48% of cases [Ancochea J. , Giron R. _ M. , 2007]. According to the results of studies in the United States, the most common causative agent of ASLT is the parainfluenza virus, type 1. During periods of epidemics, the cause of stenosis of the larynx is the influenza virus, type A [Sentsova T.B., 2004; Khaitov R. M., Pinegin B. V., 2000; Akikusa J. _ D. , Kemps A. _ S. , 2009].

Predisposing factors for the development of OSLT are the anatomical and physiological features of the children's larynx and trachea: small diameter, softness and compliance of the cartilaginous skeleton; short narrow vestibule and funnel-shaped larynx; highly located and disproportionately short vocal folds; hyperexcitability of the adductor muscles that close the glottis; functional immaturity of reflexogenic zones and hyperparasympathicotonia [Bogomilsky M.R., 2000; Britkova T.A., Lekomtseva O.I., Yuzefovich N.V., 2008; Zaitseva O.V., 2006; Karpov V.V. , Safronenko L.A. , 2005; Korovina N.A., Cheburkin A.V., Zaplatnikov A.L., Zakharova I.N., 2004]. The abundance of lymphoid tissue in young children with many mast cells, blood vessels, poor development of elastic fibers in the mucosa and submucosa quickly lead to swelling of the subglottic space and contribute to the development of OSLT. An unfavorable background is atopy (children with an atopic phenotype may have a predisposition to laryngeal edema and recurrence of croup against the background of acute respiratory viral infections), drug allergies, anomalies in the structure of the larynx, accompanied by congenital stridor, paratrophy, perinatal CNS damage, prematurity [Kladova

O.V., 2003; ON THE. Geppe, A.B. Malakhova, 2012 ; Krivitskaya V.Z., Sominina A.A., Voitsekhovskaya E.M., Sukhovetskaya V.F., 2002; Nauman W. _ H. , 2001].

The narrowing of the garter space causes a violation of the drainage function of the respiratory tract, the concentration of tracheobronchial contents. This, in turn, increases the cough, which leads to a spasm of the muscles of the larynx. The result is an increase in hypoxia. At this stage, the inflammatory process in the larynx and trachea is catarrhal or catarrhal-purulent. The ineffectiveness of conservative therapy makes it necessary to resort to the toilet of the tracheobronchial tree, prolonged intubation, tracheostomy. The consequence of such an intervention is trauma to the mucous membrane and the possible development of obstructive stenosing laryngotracheobronchitis [Krasnov VV, Anastasiev VV, Zmachinskaya TB, 2002; Syromyatnikov D.B., 2004; Feklisova L.V., Novokshonova V.A., Shebekova V.M., 2005].

Of great importance in the development of acute laryngotracheitis is the premorbid state: exudative-catarrhal and thymic-lymphatic diathesis, prematurity, aggravated obstetric anamnesis, artificial feeding, sepsis, pneumonia, ARVI transferred during the neonatal period; vaccination during SARS [Spiridonova E.A., Lobushkova I.P., 2009; Feklisova L.V., Novokshonova V.A., Shebekova V.M., 2005] .

As a result of a viral infection, inflammatory edema occurs with cellular infiltration of the vocal cords, mucosa of the garter space, trachea and adjacent tissues, accompanied by hypersecretion of the mucous glands and the accumulation of thick sputum in the airway lumen, as well as reflex laryngospasm. The presence of thick sputum in the lumen of the respiratory tract, edema and inflammatory changes in the mucous membrane of the larynx, including in the region of the vocal folds, lead to a violation of the closure of the vocal folds during phonation and cause dysphonia [Britkova T.A., Lekomtseva O.I. , Yuzefovich N.V., 2008; Zaitseva O.V., 2006; Karpov V.V. , Safronenko L.A. , 2005].

Currently, the dual nature of acute laryngotracheitis is distinguished [Arifov S.S., Umarova Sh.T. K., 2005]:

- occurs as a clinical manifestation of the actual viral infection;

- occurs as a complication of SARS caused by secondary bacterial microflora.

The primary etiological factor is always respiratory viruses, and the bacterial flora often joins, modifying the course of the disease, which determines its outcome. Respiratory viruses as a cause of acute laryngotracheitis can be distributed as follows: influenza viruses - 56.8%, parainfluenza viruses - 20.1%, adenoviruses - 16.7%, mixed viral infection - 6.4% [Sukhovetskaya V. F., Monaenkov A.O., Milkint K.K., Sominina A.A., 2002].

Pathogenesis in OCJIT of viral etiology, it is determined by the addition of bacterial complications , the development of severe pneumonia, sepsis. In crops separated larynx and trachea, the growth of S. auveus is found in association with hemolytic streptococcus, St. pneumoniae, H. influenzae, B. Catarrhal [Sergeeva S. A., Kladova O. V., Uchaikin V. F., 2002]

In the course of the study , S. N. Orlova (2006) revealed the role of individual endo- and exogenous factors in the formation of recurrent stenosing laryngotracheitis and the features of its course. The influence of the composition of the microflora of the main loci of the body, connective tissue dysplasia, regulatory systems on the function of external respiration, the formation of threshold sensitivity and reactivity of the respiratory tract in children with RSLT has been proven. Risk criteria for the occurrence and recurrent course of CJIT, diagnostic criteria for verifying the nature of the threshold sensitivity of the respiratory tract have been developed [Kalistratova E. P., Orlova S. N., Tyurina M. V., 2003; Ovsyannikova E.M., 2007; J. Holt, N. Krieg, P. Snita, J. Staley, S. Williams, 2007; P. Kostinov, 2001; Radtsig E.Yu. , 2007].

The pathogenesis of acute laryngotracheitis is inextricably linked with the pathogenesis of ARVI as a whole. Acute laryngotracheitis syndrome is character-

ized by three main symptoms: voice change, rough cough, stenotic breathing. Stenosis of the lumen of the larynx and trachea is due to the following components: edema and infiltration of the mucous membrane; spasm of the muscles of the larynx and trachea; hypersecretion of the glands of the mucous membrane of the trachea and bronchi, the concentration of thick mucopurulent secretions [Alenina T. M., Karavaev V. E., 2002; Afanasiev O.I., 2006; Belousov Yu.B., Karpov M.V., Leonova M.V., Efremenkov O.V., 2006; Zaitseva O.V., 2006; Zaplatnikov A.L., 2004; Krasnov V. V., Anastasiev V. V., Zmachinskaya T. B., 2002; Feklisova L.V., Novokshonova V.A., Shebekova V.M., 2005].

The development of acute laryngotracheitis syndrome begins with inflammation of the mucous membrane of the larynx and trachea, the most striking manifestation of which in the larynx is swelling of the garter space, and in the trachea - hypersecretion of the glands.

The role of the external environment (climate, season of the year) and its pollution in the development of OCLT is noted in the literature [Belousov Yu.B., Karpov M.V., Leonova M.V., Efremenkov O.V., 2006; Parshin V.D., 2001; Sukhovetskaya V.F., Sominina A.A., Drinevsky V.P., Milkint K.K., 2004], but there is no analysis of the consequences of their combined impact on pathogenesis stenosis.

The works of many authors are devoted to the development and refinement of the main links pathogenesis OCJIT [Arifov S.S., Daliev A.G., 2009; Sukhovetskaya V.F., Milkint K.K., Sominina A.A., Krivitskaya V.Z., 2003; Khaitov R. M., Pinegin B. V., 2000].

At the same time, many aspects of the pathogenesis of acute stenosing laryngotracheitis in children remain insufficiently studied. Contradictory results of the study immunological status in patients with OCJIT, there is a multidirectional interpretation of indicators cellular and humoral links of immunity, nonspecific protection factors [De soto H. , 2008; Nishicava T. , Haniki A. , 2003].

V. V. Lazarev (2003) obtained data indicating that etiological the basis of primary and recurrent forms of acute stenosing laryngotracheitis are respiratory viruses, microbial associations, chlamydia or their combinations. Risk factors for the occurrence and development acute stenosing laryngotracheitis in children are: weighed down on atopy, heredity, male gender, early age of the child, poor nutrition and upbringing of children, and, especially, frequent respiratory diseases [Abdullaeva N.N., Tajibaev G.A. , 2014; Abdullaeva N.N., Khodzhaeva K.A. Zakirova Sh.A. , 2002; Britkova T.A., Lekomtseva O.I., Yuzefovich N.V., 2008; Ezhova M.N., 2007].

Established predominance allergic component in the pathogenesis of acute stenosing laryngotracheitis , developing and proceeding against the background of secondary immunodeficiency and increase the tone of the parasympathetic department vegetative nervous system [Bashkina OA, 2006].

The influence of a burdened allergic anamnesis on the incidence of airway obstruction has been confirmed by a number of studies [Golubtsova E.E., Savenkova M.S., Afanas'eva A.A., 2001; Zaitseva O.V., 2006; Zaplatnikov A.L., 2004; Sergeeva S. A., Kladova O. V., Uchaikin V. F., 2002].

S. S. Arifov et al. (2009) proved that OSLT proceeds with vegetative disorders, which, in turn, have a significant impact on the course and outcome of the underlying disease [Arifov S.S., Daliev A.G., 2009].

It turned out that endocrine dysfunction in children with the primary form of acute stenosing laryngotracheitis is manifested by a combination of normal levels hormones thyroid gland with high thyroid-stimulating activity hormone and low concentration cortisol , and in the recurrent form disease there is a normal level of triiodothyronine and elevated values thyroxine , thyroid-stimulating hormone and serum cortisol blood [Uchaikin V.F., Kharlamova F.S., Savenkova M.S., Afanas'eva A.A., 2000; Feklisova L.V., Spiridonova E.L., Lobushkova I.P., 2009].

In the work for the first time it was proved that the use of low-intensity laser radiation in combination with bacterial immunomodulators of vaccine action in the

treatment of acute stenosing laryngotracheitis leads to rapid regression symptoms of the disease, reduces the length of stay of patients in hospital and reduces the need to use antibiotics , hormones and other medications. It has been shown that children with recurrent form of acute stenosing laryngotracheitis in the presence of signs of vagotopia is shown preventive treatment according to the original method using low-intensity laser and LED radiation in combination with bacterial immunomodulators of vaccine action [Taits BM, 2005].

M. Ya. Studenikin et al. (2002) [Sukhovetskaya V.F., Sominina A.A., Drinevsky V.P., Milkint K.K., 2004] prove the predominance of allergic component in the pathogenesis of the disease documented by the fact that in the primary and recurrent acute stenosing laryngotracheitis in more than 90% of sick children, an increased level of general and allergen-specific IgE. An increased content of eosinophils in blood was detected 1.5 times more often in children with the primary form, and an increased content of auto-rock was 2 times more common in recurrent form of acute stenosing laryngotracheitis [Sukhovetskaya V.F., Sominina A.A., Drinevsky V.P., Milkint K.K., 2004].

In recent years, the role of specific and nonspecific factors of immune defense has been given great importance in the pathogenesis of OSLT.

The state of nonspecific protection in OSLT is characterized by a decrease in the phagocytic activity of leukocytes, the absence of complement activation at a high level of CEC, a low level of properdin and lysozyme, which correlates with the severity of the process [Orlova S. N., Ryvkin A. I., Pobedinskaya N. S., Alenina G.M., 2003].

OSLT reveals significant changes in the cellular link of immunity , which are expressed in a decrease in the total content of T-lymphocytes, primarily T-suppressors, with minor changes in the content of B-lymphocytes. This indicates the presence of secondary immunological deficiency in OSLT, which leads to the progression of the process, an increase in allergy phenomena [Belousov Yu.B., Karpov M.V., Leonova M.V., Efremenkov O.V., 2006; Karpov V.V., Safronenko

L.A., Shapranov N.L., 2000; Kondratieva, E.I., 2007; Fonseca S. V., Irisi S. , 2009; Nishicava T. , Haniki A. , 2003].

The state of humoral immunity in OSLT is characterized by dysimmunoglobulinemia [Dick G.A., 2005; Karpov V.V. , Safronenko L.A. , 2005; Medvedeva T.V., Meshkova R.Ya., Yasnetsova A.F., Shevtsova N.S., 2000; Gaffey M. _ G. , Kaiser D. _ L. , Hayden F. _ G. , 2008; Wade S. , 2005]. M.Ya. Studenkin et al. (2002), like most researchers, note a decrease in Ig A and Ig G [Sukhovetskaya V.F., Sominina A.A., Drinevsky V.P., Milkint K.K., 2004] in combination with an increased level of Ig M [Nikulin, B.A., 2005; Orlova S. N., Alenina G. M., Karavaev V. E., Berdunova E. G., 2005; Stazhadze L.L., Spiridonova E.A., Feklisova L.V., Lobushkova I.P., 2009; Akikusa J. _ D. , Kemps A. _ S. , 2009; Volosovets A.P., Krivopustov S.P., 2007]. Downtrend Ig M occurs mainly in uncomplicated OSLT [Nikulin, B.A., 2005; A.A. Baranov, A.V. Gorelov, B.S. Koganov, N.A. Korovina, K. Tatochenko, V.F. Uchaikin, 2002; Shcherbakova A.A., Kharlamova F.S., Kladova O.V., Kharlamova F.S., Suskova V.S., 2005].

According to Yu.V. Mitina (1986), the implementation of ARVI in the form of stenosing laryngotracheitis occurs against the background of a decrease in Ig M and Ig G , while Ig A is determined at a sufficiently high level during the entire period of the disease .

Of great interest are works on the determination of Ig E in order to identify - the role of atopy in the pathogenesis of OSLT [Balabolkin I.I., 2011 ; Galustyan A. N., Martynkin A. S., 2008 ; Veltishchev Yu.E. , 200 6; Sukhovetskaya V.F., Sominina A.A., Drinevsky V.P., Milkint K.K., 2004 ; Gwalthney JMJr ., Winter B. , Patrie JT , Hendley JO ., 2012].

M. Ya. Studenikin (2002) found high levels of Ig E in all patients with OSLT in ARVI, which coincides with the opinion of other authors [Balabolkin I.I., 2011 ; Sukhovetskaya V.F., Sominina A.A., Drinevsky V.P., Milkint K.K., 2004].

Yu.E. Veltishchev (200 6) also believes that the development of OSLT (pseudocroup) in parainfluenza infection is associated with a significant increase in Ig titer E and specific Ig And in nasopharyngeal secrets in children with SARS [Veltishchev Yu.E. , 2006] .

These studies, given that elevated levels of Ig E is a pathogenic marker of atopic diseases, emphasizing the important role of the reagin mechanism in the occurrence of OSLT [Balabolkin I.I., 2011 ; Balkarova E. O., Chuchalin A. G., Gracheva N. M., 2010 ; Galustyan A. N., Martynkin A. S., 2008 ; Veltishchev Yu.E. , 200 6; Sukhovetskaya V.F., Sominina A.A., Drinevsky V.P., Milkint K.K., 2004].

Due to the occurrence, viral, bacterial and mixed (viral-bacterial) laryngotracheitis are distinguished [Orlova S. N., Alenina G. M., Karavaev V. E., Berdunova E. G., 2005; Sentsova T.B., 2004; Stazhadze L.L., Spiridonova E.A., Feklisova L.V., Lobushkova I.P., 2009; Sukhovetskaya V.F., Monaenkov A.O., Milkint K.K., Sominina A.A., 2002; Khaitov R. M., Pinegin B. V., 2000; Shaitor V. M., Melnikova I. Yu. , 2007 ; Akikusa J. _ D. , Kemps A. _ S. , 2009; Volosovets A.P., Krivopustov S.P., 2007; Van - Bever H. _ P. , Wierinda M. _ H. , 2005].

In the course of the inflammatory process, acute and chronic laryngotracheitis are distinguished. Acute laryngotracheitis lasts several weeks and ends with complete recovery. With adverse concomitant factors, it can take a protracted course and turn into chronic laryngotracheitis, which is characterized by a long course with periods of remission and exacerbations, which often occur in the autumn-winter period.

Depending on the ongoing morphological changes in otol and ringology, chronic laryngotracheitis is classified into types: catarrhal, hypertrophic and atrophic [Smirnov V . C. _ , 2004; Stazhadze L.L., Spiridonova E.A., Feklisova L.V., Lobushkova I.P., 2009; Sukhovetskaya V.F., Monaenkov A.O., Milkint K.K., Sominina A.A., 2002].

In acute laryngotracheitis, there is a pronounced hyperemia of the mucous membrane of a bright red hue, accumulation in the lumen of the larynx and trachea

of a large amount of purulent exudate, thickening of the mucous membrane due to its impregnation with exudative fluid. In the initial period of laryngotracheitis, the exudate has a liquid consistency, as the disease develops, it thickens, fibrinous films appear on the mucosa. In the case of strepto- or staphylococcal etiology of laryngotracheitis, the formation of yellow-green crusts is observed, filling the lumen of the respiratory tract [Bashkina O. A., Aleshkin V. A., Afanasyev S. S., Vorobyov A. A., Boyko A. V., Krasilova E.V., 2003].

The catarrhal form of chronic laryngotracheitis is characterized by hyperemia of the mucosa with a congestive cyanotic tint, thickening of the mucosa due to its infiltration, expansion of the submucosal vessels and the presence of small punctate (petechial) hemorrhages in the submucosal layer due to increased vascular permeability [Tatochenko V.K., Dorokhova N.F., Shmakova S.G., 2006].

In chronic hypertrophic laryngotracheitis, there is hyperplasia of the mucosal epithelium, connective tissue elements of the submucosal layer and mucous glands, infiltration of the fibers of the internal muscles of the larynx and trachea, including the muscles of the vocal cords. Thickening of the vocal cords in hypertrophic laryngotracheitis may be diffuse or have limited localization in the form of nodules [Markova, T.P., 2007].

The atrophic form of chronic laryngotracheitis is accompanied by the replacement of the cylindrical ciliated epithelium of the mucosa with flat keratinizing, sclerosis of the connective tissue elements of the submucosal layer, atrophy of the intralaryngeal muscles and mucous glands. There is thinning of the vocal cords, drying of the secretion of the mucous glands in the form of crusts covering the walls of the larynx and trachea [Lobushkova I.P., Spiridonova E.A., 2009].

V. F. Uchaikin (2001) recommends distinguishing primary, repeated and recurrent OSLT, taking into account the degree of atopy increase and the number of episodes of the disease in history [Tuffaha A. , Gern J. _ E. , Lemanske R. _ F. , 2000].

A feature of the current course of OSLT is their tendency to relapse [Golubtsova E.E., Savenkova M.S., Afanas'eva A.A., 2001; Dick G.A., 2005; Karpov V.V., Safronenko L.A., Shapranov N.L., 2000; Kondratieva, E.I., 2007; Ovsyannikova E.M., 2007; Ostrovsky S. G., 2001]. Some authors even propose to distinguish OSLT with a recurrent course as an independent clinical and pathogenetic form of the disease [Sukhovetskaya VF, 2004].

Recurrence mechanisms are based on a significant change in the - immunological reactivity of the body, associated with its allergization by both infectious and non-infectious agents, including adverse environmental, seasonal, meteorological and even social conditions [Belousov Yu.B., Karpov M.V., Leonova M. .V., Efremenkov O.V., 2006; Parshin V.D. , 2001; Sukhovetskaya V.F., Sominina A.A., Drinevsky V.P., Milkint K.K., 2004] .

The most modern and comprehensive is the clinical classification of acute laryngotracheitis proposed by Yu. V. Mitin.

I. Type of respiratory viral infection:

- influenza, parainfluenza, adenovirus infection, etc.;

- ARVI (indicated if clinical interpretation is impossible and there is no express diagnostics).

II. Form and clinical variant:

- primary form;

- recurrent form.

III. Flow:

- continuous;

- wavy.

IV. Stage of stenosis of the larynx:

- compensated;

- incomplete compensation;

- decompensated;

- terminal.

Based on this classification, the diagnosis should be formed as follows: “Acute respiratory viral infection. Primary acute laryngotracheitis, 1st variant, continuous course. Stenosis of the larynx in the stage of incomplete compensation. "Flu. Recurrent acute laryngotracheitis, 2nd variant, continuous course. Compensated stenosis of the larynx" .

Acute laryngotracheitis develops in young children - mostly from 6 months. up to 3 years. In children under the age of 4 months. this disease practically does not occur, at the age of 4 to 6 months. isolated cases are observed, the highest incidence occurs in the 2nd half of the child's life. Boys get sick almost 3 times more often than girls. This indicates the importance of the characteristics of the reactivity of the organism of children of this age, as well as the fact that a narrow glottis in children is not the main factor in the development of laryngeal stenosis [Tsypin L.E., 2007].

In recent years, there has been a clear trend towards an increase in the frequency of repeated episodes of laryngotracheitis in children, which not only complicates the course of a respiratory disease, but can also lead to a life-threatening condition (“false” croup) [Belousov Yu.B., Karpov M.V. ., Leonova M.V., Efremenkov O.V., 2006; Britkova T.A., Lekomtseva O.I., Yuzefovich N.V., 2008; Dick G.A., 2005; Karpov V.V., Safronenko L.A., Shapranov N.L., 2000; Kondratieva, E.I., 2007; Kladova O.V., 2003; Radtsig E.Yu. , 2007; Snisar V.I., 2009; Mazzaglia G. _ Caputi A. _ P. , Rossi A. , 2003].

The recurrence of OSLT in childhood contributes to the formation of chronic inflammatory processes and hyperreactivity of the upper respiratory tract, negatively affects the maturation of the child's immune system, which leads to the development of secondary immunosuppression [Veltishchev Yu.E. , 200 6 ; Zaitseva O.V., 2006; Zaplatnikov A.L., 2004; Nishicava T. , Haniki A. , 2003; Wade S. , 2005; Williams J. _ V. , Harris P. _ A. , Tollefson S. _ J. , 2014].

Thus, each new respiratory infection provokes more and more serious disorders of the immune system, contributing to the formation of both chronic inflammatory diseases of the pharynx and respiratory allergies.

1.2. Microbiocenosis of the mucous membranes of the respiratory tract in children with acute stenosing laryngotracheitis

Acute respiratory infections are the most common in childhood. Their share, together with influenza, is at least 70% in the structure of all morbidity in children. Acute stenosing laryngotracheitis is one of the most formidable manifestations of acute respiratory diseases in young children, requiring hospitalization of the child and intensive care [Armario A. , - 2006].

Some infectious agents such as respiratory syncytial virus, herpetic group of viruses, *Chlamydia pneumoniae , Myco plasma pneumoniae* persist in the body of children for a long time, contributing to the development of chronic infectious diseases of the respiratory tract. Exposure to infectious agents leads to damage to the ciliary epithelium and a weakening of its connection with the basal cells and basement membrane, which contributes to the penetration of allergens and other inflammatory stimulants into the submucosal layer [Arifov S.S., Umarova Sh.T. K., 2005; Ryvkin A. I., Pobedinskaya N. S., Orlova S. N., 2003; Stadler E. R., Keltsev V. A., Santalova G. V., Revtovich O. N., 2002; Ancochea J. , Giron R. _ M. , 2007; Daele J. , Zicot A. _ F. , 2007].

Gradual colonization of the newborn organism by microorganisms begins in the process of childbirth and continues after the birth of the child under the influence of the external environment. The formation of a biocenosis is one of the mechanisms for adapting a child to new conditions of extrauterine life [Cetinkaya F. , Tufekci b . S. , Kutluk G. , 2011 ; Emre U. , 2005; Mazzaglia G. _ Caputi A. _ P. , Rossi A. , 2003]. Pathological primary microbial colonization of various loci leads to a decrease in local immunity, allergization of the body, contributes to the formation of chronic diseases, which negatively affects the health of the child in the future [Ermakova M.K., Matveeva L.P., Yasavieva R.I., 2008 ; Arifov S.S., Umarova Sh.T. K., 2005; Tsarkova S.A., Tarina T.V., Starikova M.G., 2002].

In recent years, many countries have seen an increase in the resistance of pathogens of respiratory infections. Obviously, a change in the sensitivity of microorganisms requires changes in empirical antibiotic therapy, which is possible only if there are data obtained from constant monitoring of resistance, not only in the country as a whole, but primarily at the regional level [Kalistratova E.P., Orlova S. N., Tyurina M. V., 2003; Orlova S. N., Ryvkin A. I., Pobedinskaya N. S., Alenina G. M., 2003].

It is believed that respiratory viruses not only have a high affinity for certain parts of the respiratory tract, but also contribute to the colonization of the mucous membrane of the respiratory tract by bacteria [Abdullaeva N.N., Khodzhaeva K.A. Zakirova Sh.A. , 2002; Amosova I.V., Monaenkov A.O., Milkint K.K., 2002; Markova, T.P., 2007; Orlova S. N., Alenina G. M., Karavaev V. E., Berdunova E. G., 2005].

Viral-bacterial associations lead to a complicated course of laryngotracheitis, the formation of recurrent forms [Britkova T.A., Lekomtseva O.I., Yuzefovich N.V., 2008; Dick G.A., 2005; Karpov V.V., Safronenko L.A., Shapranov N.L., 2000; Kostinov, M.P., 2002; A.A. Baranov, A.V. Gorelov, B.S. Koganov, N.A. Korovina, 2002; Pobedinskaya N. S., Orlova S. N., 2000; Henderson A. _ J. , Arnott J. , Young S. , 2005]. Most domestic pediatricians note that the main bacteria detected during RT are opportunistic pneumotropic microorganisms, which are representatives of the normal flora of the respiratory tract [Pobedinskaya N. S., Orlova S. N., 2000; Syromyatnikov D.B., 2004].

Studies have shown that children with allergic diathesis, food allergies, patients with atopic dermatitis, hay fever, often and long-term ill children sensitized by previous infections, drugs, as well as in the post-vaccination period [Ryvkin A.I., Pobedinskaya N.S., Orlova S.N., 2003]. Patients with a burdened history of allergic and some other diseases are particularly prone to recurrence of laryngitis / laryngotracheitis and a protracted course of the disease [Pobedinskaya N. S., Orlo-

va S. N., Svyatova N. D., 2000; Sukhovetskaya V.F., Monaenkov A.O., Milkint K.K., Sominina A.A., 2002].

T.A. Sidorova c c oavt. (2007), stenosing laryngitis / laryngotracheitis (croup) against the background of acute respiratory infection is currently considered as a manifestation of respiratory allergy against the background of airway hypersensitivity to infectious and non-infectious allergens [Solovyeva M. N., Shcherbakova A. A., Kladova O. V., 2005].

The analysis of literature data showed that a significant proportion of children with repeated episodes of laryngitis have underlying allergic diseases (atopic dermatitis, allergic rhinitis, bronchial asthma) [Ryvkin A.I., Pobedinskaya N.S., Orlova S.N., 2003; Tarasov D.I., Ababii I.I., 2004; Uchaikin V.F., Kharlamova F.S., Savenkova M.S., Afanaseva A.A., 2000; Feklisova L.V., Novokshonova V.A., Shebekova V.M., 2005; Feklisova L.V., Spiridonova E.L., Lobushkova I.P., 2009]. However, despite the fact that in the etiology of OSLT, especially recurrent, infectious and non-infectious factors, in particular allergic, are important, the diagnosis of the latter has so far been covered only fragmentarily [Ryvkin A.I., Pobedinskaya N.S., Orlova S.N. , 2003].

A sufficiently large percentage of etiologically undeciphered OSLT may indicate that not only the microbial factor plays a role in the pathogenesis of the disease, but there are other factors that contribute to and lead to the development of a picture of laryngitis and stenosis of the larynx in a child. These conditions include climatic and seasonal factors. According to long-term observations, the peak incidence of OSLT occurs in the autumn-winter period (50%), in spring this percentage decreases to 30%, in summer it is about 16-20% [Belousov Yu.B., Karpov M.V., Leonova M.V. , Efremenkov O.V., 2006; Parshin V.D., 2001; Sukhovetskaya V.F., Sominina A.A., Drinevsky V.P., Milkint K.K., 2004].

Some authors attribute an increase in the incidence of OSLT to dry weather against the background of increased wind flows and dust storms [Sukhovetskaya V.F., Sominina A.A., Drinevsky V.P., Milkint K.K., 2004]. It is noted that the

largest number of admissions to the hospital for acute stenosing laryngotracheitis and its complicated forms was recorded from the most polluted industrial areas, places of maximum concentration of transport [Khaitov R. M., Pinegin B. V., 2000]. Some researchers have established a direct relationship between the OSLT frequency and the increased content of nitrogen dioxide ($N0_2$) and dust in the air [Tarasov DI, Ababii II, 2004].

W. _ W. _ Busses J. _ A. _ (2008), analyzing the reasons for the steady increase in OSLT in ARVI, points to the aggravating role of factors such as dry atmospheric air at home, which has an irritative effect on the respiratory system.

1.3. Diagnostic methods for acute stenosing laryngotracheitis

For the etiological interpretation of ARVI in modern conditions, the methods of enzyme immunoassay, immunofluorescence, radioimmunoassay, immunoelectron microscopy, serological, virological methods are used. In the first days of the disease, as a rule, the method of immunofluorescence is used - the detection of virus antigens in the cytoplasm of the epithelial cells of the nose and nasopharynx. Less common in clinical practice are serological tests based on the determination of an increase in antibody titer in paired sera in the complement fixation reaction (CFR), neutralization reaction (RN), and hemagglutination inhibition reaction (HITA) [Taits B.M., 2005; Tarasov D.I., Ababii I.I., 2004, Uchaikin V.F., Kharlamova F.S., Savenkova M.S., Afanaseva A.A., 2000; Feklisova L.V., Novokshonova V.A., Shebekova V.M., 2005; Feklisova L.V., Spiridonova E.L., Lobushkova I.P., 2009; ON THE. Korovina, Zaplatnikova A . M. , 2001].

However, the above methods of laboratory diagnostics are not able to meet the needs of science and practical medicine at the present stage. So, a significant drawback of serological diagnosis is its retrospective nature, since in order to accurately confirm the diagnosis, it is necessary to establish an increase in the titer of specific antibodies in the dynamics of the disease, for which the first serum is tak-

en at the onset of the disease, and the second - after 7-14 days and later [Sukhovetskaya V. F., Milkint K.K., Sominina A.A., Krivitskaya V.Z., 2003].

Analyzing the studies of the viral etiology of laryngitis, it should be noted that such an evidence-based diagnostic method as the detection of DNA or RNA of respiratory viruses based on the results of polymerase chain reaction (PCR) is not common in domestic clinical practice. The study of the etiological spectrum using modern diagnostic methods (luminescent, serological, PCR) in the genesis of both acute and recurrent forms of laryngotracheitis would clarify the content and direction of etiotropic therapy (antibacterial, antiviral) [Abdullaeva N.N., Khodzhaeva K.A. , Nadzhimutdinova N.Sh. , 2005].

For the isolation and identification of bacterial pathogens, bacteriological inoculation of material on selective media is widely used [Tarasov D.I., Ababii I.I., 2004; ON THE. Korovina, Zaplatnikova A . M. , 2001]. However, as the analysis shows, most pediatricians and infectious disease specialists do not always include this method in the mandatory diagnostic algorithm for RT. At the same time, bacteriological studies are necessary, given the fact that the etiological factor of recurrent laryngotracheitis is most often a viral-bacterial mixed infection. The need for bacteriological examination of children with acute and recurrent laryngotracheitis increases due to frequent microbial infection of children in the interrecurrent period of the disease [Orlova S. N., Alenina G. M., Karavaev V. E., Berdunova E. G., 2005; Smirnov B . C. _ , 2004; Sukhovetskaya V.F., Monaenkov A.O., Milkint K.K., Sominina A.A., 2002; Khaitov R. M., Pinegin B. V., 2000; Akikusa J. _ D. , Kemps A. _ S. , 2009; Volosovets A.P., Krivopustov S.P., 2007].

In foreign literature, the following forms of OSLT are distinguished: laryngotracheitis, laryngotracheobronchitis, laryngotracheobroncho-pneumonia, spastic croup and bacterial tracheitis [N.A. Korovina, Zaplatnikova A . M. , 2001]. Despite the clinical picture inherent in each of these forms, the only reliable criterion and differential diagnosis, according to these authors, is laryngoscopy.

Laryngoscopy is a method of examining the larynx through the mouth. There are two types of laryngoscopy - indirect, or mirror, and direct, or autoscopies.

The presence of flexible optics allows fibrolaryngoscopy , which a number of authors consider the most suitable for examining the larynx of children, especially young children [Bogomilsky M.R., Garashchenko T.I., 2007; Galustyan A. N., Martynkin A. S., 2008]. However, obtaining a high-quality image of the structures of the larynx using thin flexible optics (diameter 2,7 мм) is quite difficult.

1.4. Modern methods of treatment of acute stenosing laryngotracheitis

When analyzing the literature on the treatment of OSLT , the largest number of different views of clinicians on this problem was found [Belousov Yu.B., Karpov M.V., Leonova M.V., Efremenkov O.V., 2006 ; Bogonosov N.V., 2000; Voronov A.A., Volodina N.N., Samsygina T.A., 2007; Kondratieva, E.I., 2007; Kostinov, M.P., 2002].

A necessary condition for the successful treatment of OSLT is the mandatory transportation of the child to the hospital. Children with compensated and subcompensated ASLT should be hospitalized in the infection control departments of children's hospitals. Treatment of decompensated forms is carried out in intensive care units [Blokhin BM, 2009 ; Lobushkova I.P., Spiridonova E.A., 2009; Lobushkova I.P., Troitskaya N.B., Spiridonova E.A., Feklisova L.V., Blokhin B.M., 2010 ; Sabitov A.U., Starikova M.G., Zykova S.N., 2000].

A number of authors adhere to the point of view that a specialized laryngitis department based on a multidisciplinary children's hospital is the most rational form of providing assistance to patients with acute laryngotracheitis [Blokhin B.M., 2009 ; Lobushkova I.P., Troitskaya N.B., Spiridonova E.A., Feklisova L.V., Blokhin B.M., 2010 ; Sabitov A.U., Starikova M.G., Zykova S.N., 2000 ; Starikova M.G., 2001].

In recent years, various methods have been proposed for the treatment of children with acute respiratory viral infection, which occurs with symptoms of stenosing laryngotracheitis. So far, questions about the appropriateness of certain methods of treatment are being discussed [Abdullaeva N.N., Tajibaev G.A. , 2014; Abdullaeva N.N., Khodzhaeva K.A. Zakirova Sh.A. , 2002; Arifov S.S., Umarova Sh.T. K., 2005; Baranov A.A., 2006].

E.I. Karaseva (1998) used aerosol sympathomimetics and hormones (Berodual, Ingacort) in the period of acute stenotic phenomena and the anticholinergic inhalation drug ipratropium bromide (Atrovent) as the basic therapy for recurrent and severe forms of OSLT as a basic therapy to accelerate the removal and prevention of laryngoobstruction [Tsarkova S.A., Tarina T.V., Starikova M.G., 2002].

the same time G. Koren et el (2003) write about the absence of a pronounced clinical effect from fluticasone inhalations in patients with OSLT, explaining this by the deposition of a large amount of the drug in the upper respiratory tract [Nauman W. _ H. , 2001].

In addition, it must be remembered that glucocorticoids, especially when - changed for a long time and in high doses, cause hormonal immunosuppression and the progression of the inflammatory process in the presence of bacterial flora [Dobrovoljac M. , Geelhoed G. _ C. , 2009 ; Hogg J. _ C. , 2011]. And if we take into account that, according to the majority of authors, with OSLT in the stage of laryngeal stenosis I - II it is possible to achieve a positive clinical effect without the use of steroid hormones. One can understand why a number of authors quite legitimately object to active steroid therapy [Hogg J. _ C. , 2011].

Some researchers of pr and OSLT prescribed sedative therapy (valerian, relanium, 1-3% sodium bromide solution, pipolfen, sodium hydroxybutyrate, etc.) in order to relieve psychomotor agitation [Lobushkova I.P., 2006; Medvedeva T.V., Meshkova R.Ya., Yasnetsova A.F., Shevtsova N.S., 2000; Savenkova M.S., 2008].

There is a lot of controversy about the use of antibiotics in this disease. Data from Golubtsova E.E., Savenkova M.S., Afanasyeva A.A. showed a high prevalence of persistent chlamydial infection in children with recurrent stenosing laryngotracheitis. The authors propose to use "new" macrolides with a wide spectrum of action (including against chlamydia) - sumamed, rulid, rovamycin, josamycin (vilprafen) [Golubtsova E.E., Savenkova M.S., Afanas'eva A.A. , 2001].

VF Uchaikin et al (2009), noting that the main cause of stenosis of the larynx in children is influenza or parainfluenza infection, as an etiotropic method of treatment suggests the use of a complex homeopathic preparation aflubin. At the same time, the scientist notes that in each case, especially with croup syndrome in a child, it can be difficult to exclude the role of the bacterial flora. And the use of aflubin against the background of antibiotic therapy significantly reduces the time of its implementation and reduces the frequency of side effects of the antibiotic [Tsarkova S.A., Yastrebova E.B., Starikova M.G., 2001].

The need for immunotherapy in the period of convalescence is indicated by many authors. The duration of immunotherapy courses and the choice of the drug is determined by the presence of an etiotropic pathogen and concomitant microflora, the prevalence of the inflammatory process, the age of the child [Golubtsova E.E., Savenkova M.S., Afanasyev A.A., 2001; Deitmer T. , 2007; Fonseca S. V., Irisi S. , 2009].

V. V. Karpov et al. for the first time for the prevention of recurrence of stenosing laryngotracheitis used an 8-12 week course of nedocromil sodium (Thyled Mint, Rhone-Poulenc Rorer, France), which was highly effective in 90% of cases [Karpov V.V., Safronenko L .A., Shapranov N.L., 2000; Kondratieva, E.I., 2007].

Literature data indicate an increasing incidence of the disease among children, the lack of 100% effectiveness of existing methods of treatment and prevention, and individual rehabilitation that has not been worked out [Belousov Yu.B.,

Karpov M.V., Leonova M.V., Efremenkov O.V., 2006 ; Karpov V.V., Safronenko L.A., Shapranov N.L., 2000].

For the treatment of children suffering from recurrent stenosing laryngotracheitis, bacterial lysates were used, such as Bronchomunal and ribomunil, related to stimulants of specific and nonspecific immunity [Popovich, A . M. _ , 2004].

In complex therapy, bifiform was also used - a combined preparation, which includes natural bifidum bacteria and enterococci, fenspiride hydrochloride, which has an anti-inflammatory effect [Arifov S.S., Umarova Sh.T., 2005], retinol acetate or capsules "Triovit" containing vitamins C, E and β-carotene [Balkarova E. O., Chuchalin A. G., Gracheva N. M., 2010], phenibut is a nootropic drug that was prescribed to patients with significant impairment of the bioelectrical activity of the brain.

The technical result of the proposed method consists in choosing a therapy regimen depending on the degree of dysbiosis of the mucous membranes of the nasopharynx and oropharynx, followed by a complex effect on the microflora of the large intestine, airway hypersensitivity and impaired brain bioelectric activity in children [Ostrovsky S.G., 2001].

It was found that in children suffering from recurrent stenosing laryngotracheitis, there are significant disturbances in the composition of the microflora of the mucous membranes of the nasopharynx and oropharynx, characterized by the development of dysbiosis of I or II degree, associated disorders of the microbiocenosis of the digestive tract, forming chronic inflammation of the mucous membranes, contributing to the sensitization of the body, leading to violation of the function of external respiration and threshold sensitivity, bioelectrical activity of the brain, which causes a persistent course of the disease and justifies the need to include drugs and methods in the complex of therapy that allow correcting the identified changes [Orlova S. N., Alenina G. M., Karavaev V. E. ., Berdunova E.G., 2005].

The essence of the proposed method of treatment S. N. Orlova , A. I. Ryvkin consists in the use of 2 therapy programs, the choice of which is carried out in accordance with the revealed degree of dysbiosis of the mucous membranes of the upper respiratory tract. Sowing associations of pathogenic gram-positive microbes or Staphylococcus aureus in a monoculture characterizes the development of dysbiosis of the first degree, when determining pathogenic gram-positive microorganisms in association with pathogenic gram-negative ones, it indicates the formation of dysbiosis of the second degree [Balabolkin I.I., 2011]. Dysbiosis III and IV degree in the observed children were not recorded. The control group (20 children) consisted of patients who used basic therapy, including a hypoallergenic diet, irrigation of the mucous membranes with mineral water 4 times a day, chest massage, breathing exercises, physiotherapy - salt inhalations "Galoneb".

1 program included bronchomunal-P, bifiform, fenspiride hydrochloride ("Erespal") and retinol acetate (20 patients).

2 program - ribomunil, bifiform, fenspiride hydrochloride ("Erespal"), triovit and phenibut (10 patients) [Popovich, A . M. _ , 2004].

L. V. Kramar et al. (2009) believe that the most significant component of OSLT treatment is inhalation therapy aimed at restoring airway patency, combating exudate drying and affecting the inflammatory focus. Inhalation therapy was performed for all (100%) patients using NE-29 compression inhalers and OMRON N-U17 ultrasonic nebulizers. The frequency and duration of nebulizer therapy was determined by the severity of stenosis and ranged from 2 to 4 fifteen-minute inhalations per day. The starting drug was selected taking into account the clinical course and stage of croup. Steam and cold air inhalations were not used [Koryachkin V.A., 2004].

Local use of hormonal preparations with the help of a nebulizer accelerates the relief of laryngeal stenosis in acute stenosing laryngotracheitis by 1.5-2 times, and reduces the time of recovery and stay of patients in bed. The nebulizer has an advantage over other types of inhalers, as it forms microparticles of a certain size

and mass, facilitating their deposition at the level of the upper respiratory tract [Geppe N.A., 2000 ; Lacoste Nicholas J. _ L. , Infante Sanchez J. _ C. , Lantern Benedito M. , 2005].

The proposed method of treatment for T.V. Medvedeva and A.M. Koroleva (2005) is easy to perform, available for any infectious disease hospital equipped with simple inhalers, reduces the load of therapeutic effects on the child, as well as the load of the physiotherapy room. Due to the antiviral, immunomodulating effect of leukinferon, a decrease in the frequency of recurrence of laryngeal stenosis in children, as well as the frequency of acute respiratory viral infections, is expected. A method for treating stenosing laryngotracheitis in children, including antibacterial, hormonal, desensitizing, antispasmodic, muco-, secretolytic, enzyme therapy and inhalation administration of a drug, characterized in that leukinferon is used as a drug for inhalation administration on the first day of treatment at a dose of 10,000 IU for interferon, diluted in 5 ml of 0.9% sodium chloride solution, from the second day - physiological sodium chloride solution, and inhalations are carried out three times a day for 10 minutes with an interval of 4 hours until the disappearance of clinical symptoms (Patent No. 2144375) .

M.F. Ermachenko et al. (2010) proposed a new method of antinociceptive protection of the trachea during extubation using sodium hydroxybutyrate, prednisolone, diphenhydramine, lasix, which helps to reduce the phenomena of laryngeal edema [Ermachenko M.F., 2010]. They justified the use of sodium oxybutyrate as a means of reducing the manifestation of stress-realizing systems during extubation. The optimal dose of sodium oxybutyrate for sedation before extubation of patients with acute stenosing laryngotracheitis was selected by monitoring the levels of consciousness by changing the BIS index. They also proved that the developed method of extubation can reduce the number of post-intubation complications in patients with acute stenosing laryngotracheitis, by reducing the time spent by the endotracheal tube in the airways and early transfer of children from the intensive care unit [Ermachenko M.F., 2010].

The developed method of extubation in patients with OCJIT using drugs: sodium hydroxybutyrate, diphenhydramine, prednisolone and lasix, allows for effective antinociceptive protection of the trachea. In addition, the method of antinociceptive protection of the trachea during extubation helps to reduce the time of prolonged intubation, compared with traditional methods, by 3-5 days, and also reduces the number of post-intubation complications by 1.5-3 times [Ermachenko M.F., 2010].

The approach to choosing a complex of therapeutic and rehabilitation measures should be individual and determined by the nature of dysbiotic disorders on the mucous membranes of the upper respiratory tract and large intestine, the sensitivity of the respiratory tract and the established changes in the bioelectrical activity of the brain [Ostrovsky S.G., 2001].

Some researchers in the treatment and OSLT in order to relieve psychomotor agitation prescribed sedative therapy (valerian, relanium, 1-3% sodium bromide solution, pipolfen, sodium hydroxybutyrate, etc.) [Voronov A.A., Volodina N.N., Samsygina T.A., 2007; Karpov V.V., Safronenko L.A., Shapranov N.L., 2000; Kostinov, M.P., 2002].

Koryukina I.P. (2002) considers it necessary to use antihistamines in OSLT therapy [Sukhovetskaya V.F., Milkint K.K., Sominina A.A., Krivitskaya V.Z., 2003] Sitnikov I.G. (2003) explains the feasibility of prescribing antiserotonin drugs, Aslanyan G.G. (2005) - antikinin drugs [Arifov S.S., Umarova Sh.T., 2005].

However, it has been noted that not only sedatives, but also antihistamines and diuretics, by disrupting the evacuation of viscous secretions from the respiratory tract, relaxing the child and inhibiting the cough reflex, can contribute to a more severe course of OSLT, since viscous mucus is not removed from the respiratory tract with a weak cough. ways, and dries up in crusts. It happens difficult notice Start transition _ stenosis in asphyxia [Joshi P. , Shaw A. , Kakakios A. , Isaacs D. , 2008].

All procedures that a child needs during OSLT (laryngoscopy, examination of the throat, removal of mucus from the upper respiratory tract, injections, etc.) should be minimally sparing. Currently, tracheotomy is practically not used to restore airway patency.

For the successful treatment of stenosing laryngotracheitis, it is mandatory early hospitalization of patients in a specialized department for the management of patients with ASLT or in the somatic children's (infectious) department in the presence of an intensive care unit and intensive care [Lobushkova I.P., Troitskaya N.B., Spiridonova E.A., Feklisova L.V., 2010]. Patients with OSLT of the 3rd degree, as well as the 2nd degree, are subject to hospitalization in the intensive care unit if the course of the disease does not improve within 24-48 hours against the background of ongoing therapy adequate to the severity of the condition.

The need for immunocorrective therapy in the complex treatment of acute and recurrent laryngotracheitis may be caused by the severity of immune and immunoregulatory disorders, the polyetiology of the pathology, and the characteristics of the adaptive immune response in children.

In the literature of recent years, there is more and more evidence that it is almost impossible to cope with the growth of infectious morbidity with the help of antibiotics, antiviral and other chemotherapeutic drugs alone [Ostrovsky S.G., 2001; Ostanin A.A., 2006; Starikova M.G., 2004]. The above drugs suppress the reproduction of the pathogen, but its final elimination from the body is the result of the activity of immunity factors. Therefore, against the background of suppressed immunoreactivity, the action of antiviral, antibacterial agents will be ineffective or ineffective [Bogomilsky M.R., Garashchenko T.I., 2007; Ostrovsky S.G., 2001]. In addition, immunotherapy is of particular importance due to the increase in antibiotic-resistant 3-lactamase-producing strains, the strengthening of the role of opportunistic microbial flora in the etiology of laryngitis in children [Volosovets A.P., Krivopustov S.P., 2007].

In this regard, the interest of researchers and practitioners in drugs that affect immunity, used in the complex treatment of various pathologies of both infectious and other genesis, has now significantly increased [Lobushkova I.P., Spiridonova E.A., 2009; Lobushkova I.P., Troitskaya N.B., Spiridonova E.A., Feklisova L.V., 2010; Lukyanov S. V., Sereda E. V., Lukina O. F., Dukhalin A. S., 2003; Martynkin A.S., Ivanova R.A., Dokhalova G.M., Ivanov V.P., Kosenko I.M., 2000; Markova, T.P., 2007; 90, p.124; Ostrovsky S.G., 2001].

Immunotherapy is prescribed in combination with other drugs (antibiotics, NSAIDs). Its effectiveness depends on the correct assessment of the initial state of the patient's immunoreactivity, the nature and severity of pathological changes, the choice of the optimal drug and the scheme of its use [Ostrovsky S.G., 2001]. It is also necessary to have an idea about the mechanisms of action of prescribed drugs, their side effects, compatibility with other methods of treating laryngotracheitis, allergenic properties [Krivitskaya V.Z., Sominina A.A., Voitsekhovskaya E.M., Sukhovetskaya V.F., 2002 ; Ostrovsky S.G., 2001].

Taking into account the pathogenetic features of acute and recurrent - laryngotracheitis in children, one of the main problems of treatment should be the search for optimally effective and safe means of etiotropic, immunomodulatory therapy that is compliant for the child [Markova, T.P., 2007; Pobedinskaya N. S., Orlova S. N., 2000]. According to the requirements, drugs used in the treatment of acute and recurrent viral infections in children of various localizations must combine the properties of an inhibitor of viral reproduction and an effective stimulator of the body's immune defense in order to eliminate the inertia of a specific antiviral immune response in children [Arifov S.S. , Umarova Sh.T., 2001].

Among the whole variety of immunocorrectors, the most promising is the use of drugs from the class of recombinant interferons, in particular viferon, endogenous interferon inducers - drugs with a universally broad spectrum of action (arbidol), as well as drugs belonging to the group of thymic factors (imunofana) [

Garashchenko T. I., Bogomilsky M. R., Markova T. P., 2004 ; Korovin N.A., Zaplatnikov A.L., 2002; Milkint K.K., Sominina A.A., Golovanova A.K., 2003].

Viferon is a complex immunomodulatory and antiviral drug with a virucidal effect, as well as the ability to modulate and enhance antiviral resistance [Karpov V.V., Safronenko L.A., Shapranov N.L., 2000; Koryachkin V.A., 2004; Ostrovsky S.G., 2001; Sabitov A.U., Starikova M.G., Zykova S.N., 2000]. The composition of Viferon includes membrane-stabilizing components (vitamin E and ascorbic acid), the combination with which causes an increase in the antiviral activity of recombinant interferon, an increase in its immunomodulatory effect on T- and B-lymphocytes [Bogonosov N.V., 2000; Milkint K.K., Sominina A.A., 2003]. When exposed to exogenous interferon, the activity of natural killers, T-helpers, cytotoxic T-lymphocytes, phagocytic activity, and the intensity of differentiation of B-lymphocytes increase in the body [Koryachkin V.A., 2004; Milkint K.K., Sominina A.A., Golovanova A.K., 2003].

The listed properties of interferon allow it to effectively participate in the processes of eliminating the pathogen, preventing infection and possible complications [Korovina N.A., Zaplatnikov A.L., 2002]. Viferon is quite widely used for - the treatment of uncomplicated forms of respiratory viral infections, however, the effectiveness of its use in acute and recurrent laryngotracheitis has not been evaluated [Milkint K.K., Sominina A.A., 2003; Milkint K.K., Sominina A.A., Monaenkov A.O., 2003; Ryvkin A.I., Orlova S.N., Balikin V.F., 2004]. At the same time, given the disturbances in the interferon status that occur in acute, and especially in recurrent laryngitis / laryngotracheitis , we assume that this drug will be quite effective in the treatment of children with this pathology .

Imunofan is a drug with immunostimulating, detoxifying, hepatoprotective and antioxidant effects. Its action is based on the enhancement of phagocytosis reactions and death of intracellular bacteria and viruses, as well as the restoration of disturbed indicators of cellular and humoral immunity, by enhancing the proliferation of T-lymphocytes, increasing the production of interleukin-2, TNF -α, IFN-γ [

Ostrovsky S.G., 2001; Ryvkin A.I., Pobedinskaya N.S., Orlova S.N., 2003]. As shown by the analysis of literature data, this drug has not been previously used in acute and recurrent laryngotracheitis. However, in our opinion, the range of immunocorrective action of imunofan suggests the effectiveness of its use in the complex therapy of acute respiratory infections, in general, and in laryngotracheitis, in particular .

Recently, Arbidol has been widely used in Russia for the treatment and prevention of respiratory viral infections [Zplatnikov A.L., 2004; Sukhovetskaya V. F., 2004]. Since this drug has, in addition to virus-specific and antioxidant, also immunomodulatory and interferon-inducing effects , it seems interesting to compare the effectiveness of arbidol in L T in children with the effectiveness of the above drugs.

Arbidol is a synthetic antiviral drug that can also stimulate the synthesis of endogenous interferon, activate phagocytosis and influence the state of the T-cell link of immunity [Garashchenko T.I. , Bogomilsky M.R., Markova T.P., 2004 ; Zaplatnikov A.L., 2004; Kostinov, M.P., 2002; Sukhovetskaya V. F., 2004]. The mechanism of its antiviral action is associated with the inhibition of the translation of virus-specific proteins in infected cells, as a result of which the reproduction of viruses is suppressed. It has been established that arbidol specifically inhibits influenza A and B viruses and increases the body's resistance to other respiratory viruses. Arb idol refers to low-toxic drugs. When administered orally in recommended doses, it does not have any negative effect on the children's body [Veltishchev Yu.E. , 200 6 ; Ryvkin A.I., Orlova S.N., Balikin V.F., 2004]. The use of arbidol in ARVI is widespread, but the effectiveness of its use for the treatment of acute and recurrent laryngotracheitis has not been evaluated.

Cytokines are the main mediators of local inflammation and acute phase response at the body level [Bjornson C. , Classen M. , Williamson J. , Brant R. , 2004]. Crowe J. _ E. _ et al. (2003) found that an increase in the level of IL -lß and TNF - a in the blood serum of children in the acute period of a viral infection in

some cases has a prognostic value, and their high concentrations can persist during the period of clinical recovery [Fonseca S. V., Irisi S. , 2009].

Changes in the state of the immune system of children with OSLT, as well as the possibility of regulating these disorders with the help of cytokines, provide a basis for searching for immunological approaches to the treatment of this disease.

Currently, for the correction of identified disorders in OSLT in children, monopreparations of cytokines of both natural (human leukocyte interferon) and genetically engineered origin (reaferon) have been used, the use of which contributes to the relief of symptoms of the disease at an earlier time [Bashkina O.A., 2006; Belova O.V., 2005; Lazarev V.V., 2003].

At the same time, it is of interest to study the role of complex preparations of cytokines in the treatment of OSLT in children, given the variety of immunological disorders in this disease. Leukinferon is one of the complex-type drugs. The clinical efficacy of leukinferon in children for the immunocorrection of diseases of the bronchopulmonary system, as well as viral infections (caused by the herpes virus, hepatitis B, C, D viruses, etc.) has been shown. In these cases, the immunomodulatory effect of the drug is combined with its antiviral effect [Konusova V.G., Simbirtsev A.S., Ketlinsky S.A., 2002; Medvedeva T.V., Meshkova R.Ya., Yasnetsova A.F., Shevtsova N.S., 2000].

Due to the biological characteristics of cytokines (short half-life, short-range action, etc.), in order to achieve the greatest clinical effect of the drug, it is optimal to create a high local concentration in the area of inflammation. A similar effect can be achieved with inhalation administration of leukinferon [Medvedeva T.V., Meshkova R.Ya., Yasnetsova A.F., Shevtsova N.S., 2000].

According to T.V. Medvedeva, inhalation cytokine therapy significantly reduces the severity and duration of the main symptoms of ASLT in children with grade 1-2 laryngeal stenosis, which leads to a decrease in the clinical severity index, starting from the first day of therapy, significantly reduces the length of the patient's stay in the hospital with 8.85±1.06 to 5.29±1.29 days. The clinical severi-

ty index makes it possible to objectively and dynamically assess the severity of OSLT in children [Koryachkin V.A., 2004; Martynkin A. S., Ivanova R. A., Zakharova I. I., 2006].

The inhalation use of cytokines (leukinferon) in the complex therapy of OSLT is recommended as an effective, safe and easily performed method of treating children with grade 1-2 laryngeal stenosis, which allows to reduce the amount of therapeutic load on patients and reduce their length of stay in the hospital [Martynkin A. S., Ivanova R. A., Zakharova I. I., 2006 ; Markova, T.P., 2007; Medvedeva T.V., Meshkova R.Ya., Yasnetsova A.F., Shevtsova N.S., 2000].

In addition, the study of the cytokine, in particular interferon, status is fundamentally important for clarifying the most important pathogenetic mechanisms for the development of this pathology in childhood, which is not only an important criterion in prescribing adequate individual anti-inflammatory and immunocorrective therapy, but also, perhaps, will allow individualizing the prognosis of the disease. . This will contribute to a differentiated approach to the choice of the method of rehabilitation and anti-relapse treatment, as well as to single out children from the risk group for the occurrence of relapses of OSLT. in the future [Markova, T.P., 2007].

V.P. Vavilova et al. (2005), based on the results of a study of local immunity of the upper respiratory tract, substantiated the possibility of using LILI to reduce the incidence of acute respiratory infections. The immunomodulatory effect of the laser was confirmed by the high activity of lysozyme, an increase in the amount of total protein and SIgA . LILI stimulated the processes of spontaneous phagocytosis of neutrophils, reduced the colonization of the nasal cavity by bacteria, and increased the nonspecific and immune resistance of the child's body. However, the improvement in local immunity remained on average no more than 6 months [Vavilova V.P., Perevoshchikova N.K., Trusov S.V., 1999].

Thus, OSLT in children currently remains a serious public health problem due to their widespread prevalence and the economic damage they cause to society

as a whole and to individuals in particular. Attention is drawn to the increase in the frequency of recurrence of laryngotracheitis, which contributes to the formation of chronic pathology of the respiratory organs, can lead to a delay in the physical and psychomotor development of children, adversely affect the formation of the child's immune system, and lead to the development of secondary immunosuppression.

Despite the fact that recently the issues of immunoregulatory mechanisms, including cytokine ones, in acute and recurrent respiratory infections have been studied in detail and in depth, there is still no consensus on this issue [Sentsova T.B., 2004]. For example, there are conflicting data on changes in the level of IL - 4 in peripheral blood in AR VI [Sofer S. , Dagan R. , 2001]. Questions about the role of cytokine regulation in the immune response in children with laryngotracheitis in general, including those with recurrent course, have not been studied. Also, the possibilities of predicting the course of LT in children have not been disclosed . At the same time, the study of the significance of changes in the cytokine balance could serve to determine the prognosis of the disease, clarify the severity and the possibility of further recurrence .

Summarizing the analysis of the literature data, we can conclude that the relevance of the problem of stenosing laryngotracheitis accompanying acute respiratory viral infections is due to its high prevalence in childhood, pronounced dynamism of clinical symptoms, the possibility of rapid development of bacterial complications and death.

The modern concept of the pathogenesis of recurrent OSLT provides for the development of a pathological process as a result of the complex effect of various etiological factors, including infectious and allergic ones, however, until now, laboratory diagnostics of the latter in practice has not become widespread .

The main pathogenetic mechanisms that form respiratory disorders: swelling of the mucous membrane of the larynx and trachea, muscle spasm of the larynx , trachea and bronchi, hypersecretion of the glands of the mucous membrane of the

larynx, trachea and bronchi, become the leading ones that determine the clinic, and ultimately therapy

It should be noted that the search for new approaches to OSLT therapy, which would allow influencing both the etiological and pathogenetic mechanisms of the disease, remains relevant so far.

CHAPTER II . STUDY METHODS OF CHILDREN WITH ACUTE STENOSING LARYNGOTRACHEITIS

2.1. General characteristics of the examined children with acute stenosing laryngotracheitis

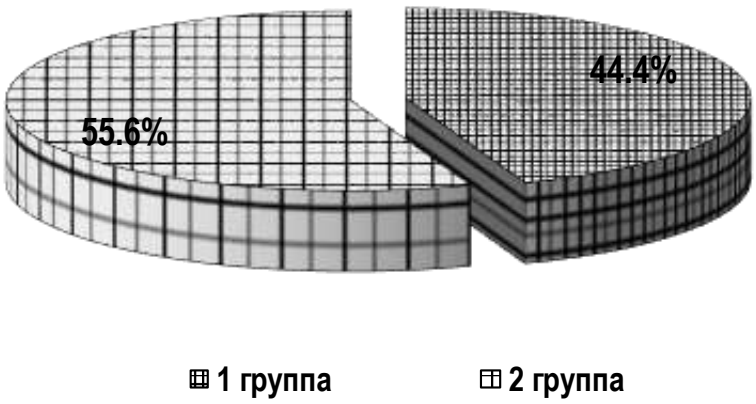
The study is based on a clinical and laboratory examination of 275 children with acute stenosing laryngotracheitis, who were under observation and admitted to the city infectious diseases hospital No. 3 in Tashkent in the period from 2011 to 2013.

The inclusion criteria for the survey were:

- age from 6 months to 5 years;
- primary and recurrent forms of OSLT;
- parental consent to the participation of the child in the study.

For an adequate assessment of the data of laboratory studies, 30 practically healthy children of comparable age were examined.

All examined children were divided into 2 groups according to the forms of acute stenosing laryngotracheitis according to the classification of Yu. V. Mitin (1986) (Fig. 2.1):

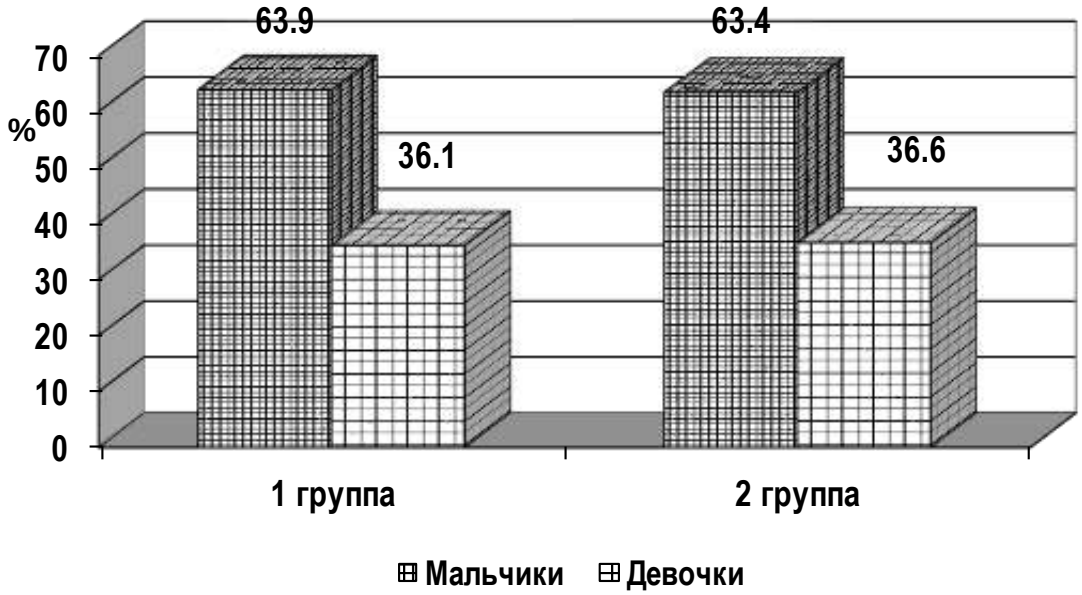


Rice. 2.1. Distribution of examined children with acute stenosing laryngotracheitis by groups

- Group 1 included 122 (44.4%) children with primary stenosing laryngotracheitis.

- Group 2 - 153 (55.6%) children with recurrent stenosing laryngotracheitis.

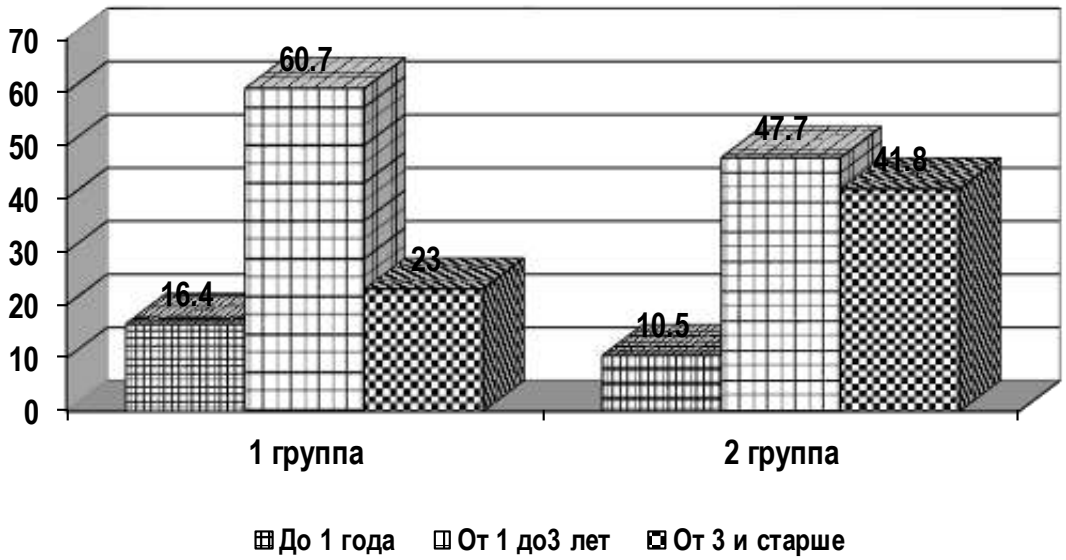
An analysis of the distribution of children with acute stenosing laryngotracheitis by gender showed that boys are more likely to get sick than girls. The ratio of girls and boys was 1:1.8 in group 1 in group 2 - 1:1.7 (Fig. 2.2).



Rice. 2.2. Distribution of examined children with acute stenosing laryngotracheitis by sex

Basically, OSLT develops in young children (from 6 months to 3 years). In group 1, the majority of children (60.7%) fell ill at the age of 1 to 3 years, and at the age of up to one year, 16.4% of children fell ill and in the period from 3 years and older - 23.0%, in group 2 the picture is somewhat different: the incidence at the age of 3 years and older is almost 3 times higher than in group 1 (Fig. 2.3).

This is due to the anatomical and physiological features characteristic of this age group, a narrow lumen of the larynx, friability of the submucosal layer in the subglottic space, abundant vascularization of the mucous membrane of the respiratory tract.



Rice. 2.3. Distribution of examined children with acute stenosing laryngotracheitis by age

In history, almost all children had ARVI, the percentage of exudative catarrhal diathesis was also high (71.3% and 69.9%, respectively, in groups), hyperthermic syndrome was observed in 53 (43.4%) children of group 1 and in 33 (21 .6%) - 2 groups. The index of past diseases in group 1 was 3.6, in the main group - 3.0, which indicates the relationship between the incidence of past diseases and the development of OSLT (Table 2.1).

Table 2.1

The structure of past diseases in children with acute stenosing laryngotracheitis

Types of diseases	1 group (n=122)		group 2 (n=153)	
	abs	%	abs	%
SARS	122	100	153	100
Exudative catarrhal diathesis	87	71.3	107	69.9
Rickets	59	48.4	41	26.8***
Hyperthermic syndrome	53	43.4	33	21.6***
Ethmoiditis	55	45.1	52	34.0
OKI	62	50.8	78	51.0

Note: * - differences relative to the data of group 1 are significant (* - P < 0.05, ** - P < 0.01, *** - P < 0.001)

An analysis of comorbidities in children with acute stenosing laryngotracheitis showed that all children had OSLT against the background of acute respiratory viral infections, and such diseases as rhinitis, tonsillitis, less often otitis media, and anemia aggravated the condition of sick children. In 2 (1.6%) children of the 1st group and in 7 (4.6%) children, febrile convulsions developed against the background of high temperature. Almost a third of sick children with ASLT were accompanied by bronchitis, pneumonia. Based on the data in this table, we conclude that a burdened premorbid background provokes the development of OSLT. Among the most common concomitant diseases of acute stenosing laryngotracheitis, a special place belongs to the diseases indicated in the table (Table 2.2).

Table 2.2

The structure of concomitant diseases in children with acute stenosing laryngotracheitis

Types of diseases	1 group (n=122)		group 2 (n=153)	
	abs	%	abs	%
SARS	122	100	153	100
Rhinitis	59	48.4	45	29.4**
Tonsillitis	fourteen	11.5	ten	6.5
Bronchitis	39	32.0	43	28.1
Otitis	7	5.7	5	3.3
Stomatitis	3	2.5	one	0.7
Anemia	57	46.7	63	41.2
Pneumonia	37	30.3	49	32.0
convulsive syndrome	2	1.6	7	4.6

Note: * - differences relative to the data of group 1 are significant (* - P < 0.05, ** - P < 0.01, *** - P < 0.001)

Patients were admitted to the hospital in the first 4 days from the onset of the disease . At the same time, in the group with recurrent laryngotracheitis, none of the patients was admitted later than 4 days from the onset of the disease, which is apparently due to the alertness that arises in parents in the event of a relapse of the disease (Table 2.3).

Spicy stenosing laryngotracheitis belongs to the group multi-factorial diseases. Its development is based on the interaction endogenous and ex-ogenous factors.

Table 2.3

Terms of admission after the onset of the disease in children with ASLT to the hospital

Timing	1 group (n=122)		group 2 (n=153)	
	abs	%	abs	%
1 day	66	54.1	82	53.6
2-4 days	46	37.7	71	46.4
More than 4 days	ten	8.2	0	0

2.2. Research methods

2.2.1. Design of studies conducted in examined children with acute stenosing laryngotracheitis

Table 2.4

Design of studies conducted in examined children with ASLT

Name of the study	Purpose of the study	materials	Method Used
General clinical and special			
Inspection of the ENT organs	Determination of the pathology of other ENT organs	-	Rhinoscopy pharyngoscopy, otoscopy
Hematological	Determination of in-dicators of peripheral blood	Blood	General clinical - blood test
Urinalysis	Determination of in-dicators of urine	Urine	General clinical - analysis of urine
Instrumental			
Laryngoscopy	Assessment of the condition of the lar-ynx	-	laryngoscopy
X-ray	Assessment of lung condition	-	X-ray of the lungs
Laboratory			
ogy	Detection of viral anti-	Epithelial cells of the	PCR

	gens in materials from the nasal cavity	lower nasal passages , nasopharyngeal secretions and aspirates	
Immunological	Determination of indicators of general and local immunity	Secrets of the oral - cavity , blood	Garib F.Yu.
Bacterioscopic	Definition of pathogenic flora	Throat and nose swabs	Romanovsky-Giemsa method
	Determination of salivary lysozyme activity	Saliva	Method V.M. Shubik
biochemical	Definition of POL-AOD	Serum	Vladimirov Yu.A., Archakov A.I.

The diagnosis of OSLT was established on the basis of a carefully collected anamnesis and analysis of complaints, the clinical picture of the disease, determining the level of immune disorders, and studying the microbiocenosis of the mucous membranes of the respiratory tract. The general clinical examination also included a thorough study of the family and allergic history of the parents.

When analyzing the history data, special attention was paid to the presence of perinatal and intranatal diseases in children. The state of health of children in the period preceding the development of OSLT was carefully studied, the features of the course of the pathological process were carefully studied.

2.2.2. General clinical studies

Upon admission of children to the hospital, a thorough examination of the patients was carried out, the general condition and severity of symptoms of - intoxication, catarrhal syndrome , etc. were assessed.

A clinical blood test was performed for all children at the time of admission and over time. The general clinical analysis of blood included the determination of hemoglobin concentration, the number of erythrocytes, the color index, the number of leukocytes, platelets, the calculation of the leukocyte formula, the determination of the erythrocyte sedimentation rate (ESR) and some other indicators that were made according to clinical indications. The hemogram acquired diagnostic value in conjunction with clinical signs [N. L. Shapranov].

A general urinalysis was performed for all sick children at the time of admission and in the dynamics of the disease.

2.2.3. Instrumental Research

Laryngoscopy - This is a method of visual examination of the larynx using a special device (laryngoscope), related to endoscopic research methods.

The examination of the larynx was carried out by direct laryngoscopy to resolve the issues of differential diagnosis of the studied pathology .

Direct laryngoscopy - direct laryngoscopy allows you to examine the internal structure of the larynx in a direct image and perform various manipulations on its structures in a fairly wide range, as well as perform emergency or planned intubation. It is based on the use of a rigid directoscope, the introduction of which into the laryngopharynx through the oral cavity becomes possible due to the elasticity and compliance of the surrounding tissues.

X-ray studies . Chest x-rays were performed in those children in whom pulmonary lesions were suspected . The studies were carried out according to the usual method: X- ray of the chest in frontal and lateral projections in the vertical position of the child.

Identification of viruses by polymerase chain reaction (PCR).

PCR studies were carried out in the laboratory of MNIL TMA in the biochemical laboratory (Abduvaliev A.A.).

The test material was transferred into a test tube with a reagent using disposable sterile probes. The tubes with the reagent containing the analyzed material were thoroughly mixed on a microcentrifuge-shaker for 10 seconds, the tube was placed in a solid-state thermostat and incubated at a temperature of +98 ^{0} C for 10 minutes.

After completion of incubation, the tubes were centrifuged at 12,000 rpm at room temperature (+18…+25 ^{0} C) for 15 sec.

The resulting supernatant was used as a test DNA sample for setting up the amplification reaction. The resulting supernatant was stored at a temperature of +2 - +8 ^{0} C for no more than one week or at a temperature of -20 ^{0} C for no more than 6 months.

PCR diagnostics of HSV I and II were carried out in accordance with the protocol for the set of the FLUOROPOL-RV format in the OneStep package .

1. Take the required number of test tubes out of the box and arrange them in accordance with the pre-prepared protocol. The reaction is carried out on the analyzer Rotor Gene -6000 (Corbet research).

2. Completely thaw the contents of the tubes. If necessary, if part of the solution is on the inside of the tube cap, centrifuge the tubes for 3-5 seconds on a microcentrifuge - vortex.

3. Add to all tubes with individual tips with aerosol filters 5 µl each:

- in a test tube of the studied samples - the studied DNA samples;

- into a test tube of a negative control sample - a diluent from the kit;

- into a test tube of a positive control sample - a positive control DNA sample from the set of the kit used.

4. Close the tubes tightly and centrifuge for 15 seconds on a microcentrifuge - vortex.

5. Create a sample location protocol. FAM (specific signal), HEX (internal control signal) channels are used to work with FLUOROPOL kits .

Detection of amplification products is carried out by the device automatically in each amplification cycle. Based on these data, the control program plots the fluorescent signal accumulation curves for each of the channels specified for the samples.

6. Transfer the tubes to the device and carry out amplification according to the following program:

+95 ^{0}C	1min 30 sec	
+95 ^{0}C	10 sec	40 cycles
+60 ^{0}C	20 sec (readout)	
+72 ^{0}C	40 sec	

In the presence of any other DNA templates, a specific fragment is not synthesized.

2.2.4. Immunological research methods

The immune status was studied in 275 children with acute laryngotracheitis using indicators of cellular and humoral immunity, namely: determination of the percentage of lymphocytes; determination of the number of T- and B-lymphocytes; determination of the subpopulation of T-lymphocytes - T-helpers and T-suppressors; The phenotype of immunocompetent cells was determined using

monoclonal antibodies C D 3, C D 4, C D 8, C D 25, C D 95 and others manufactured by Sorbent- LTD according to the method of F. Yu. Garib et al. (1988).

For research, blood is taken from the cubital vein in the amount of 3 ml per physiological solution with heparin. The blood is diluted in a ratio of 1:3 and layered on a mixture of ficoll-verografin with a solution density ingredient of 1.077 to isolate lymphocytes by sedimentation. The resulting mixture was centrifuged at 1500 rpm for 30 minutes. The resulting lymphocytic ring was aspirated into a clean tube and washed with saline twice. The volume of the solution was adjusted to 1 ml, and then the number of lymphocytes in the Goryaev chamber was determined, the number should be from 40 to 60 in 12.5 squares.

Preparation: T-, B-, H-, C-, NK-systems.

1. Human blood is taken, erythrocytes are washed and a 50% erythrocyte suspension is prepared.

2. Preparing a 0.3% solution of chromium chloride in saline.

3. Mixed in a clean tube 50 µl of 50% red blood cell mass, 50 µl of 0.3% chromium chloride solution and 3 µl of the appropriate monoclonal antibodies. The tube is shaken for 2-3 minutes, centrifuged for 2-3 minutes and the resulting suspension is washed with 3 ml of 0.9% sodium chloride solution for 10 minutes three times. The supernatant must be drained, and then the volume of the solution is brought to 1.25 ml and the mixture is resuspended.

Determination of the level of serum immunoglobulins A, M and G and immunoglobulins in peripheral blood was carried out by the simple radial immunodiffusion method according to the Mancini method. G et . al . (1965) using standard Russian-made monospecific antisera (N. I. Mechnikov Research Institute of Microbiology, Moscow).

When determining the total number of T-lymphocytes and their main subpopulations, the total number of B-lymphocytes and natural killers in the peripheral blood, we used the method of rosette formation (Garib F. Yu. et al., 1995; Zal-

yalieva M. V., 2004). To set up the rosette reaction, erythrocyte diagnosticums were preliminarily prepared using formalized human erythrocytes 1(0) of the Rh + group, which were loaded with monoclonal antibodies using 0.3% chromium chloride. To detect T (CD3) - lymphocytes, LT 3 was used, T-helpers (CD4) - LT 4, T-suppressors (CD8) - LT 8, mature B-lymphocytes (CD19) - LT 19 and natural killers (CD16) - LT 16 monoclonal antibodies produced by the Institute of Immunology of the Ministry of Health of Russia (Moscow).

Venous blood was taken on heparin (24 U/ml), layered on a ficoll-verografin density gradient (1.077 g/ml) and centrifuged at 1500 rpm for 30 min. The lymphocytes obtained in the interphase were transferred into a clean test tube, washed three times with medium 199 by centrifugation at 1000 rpm for 10 min, and the cell concentration was adjusted to 2 million/mL. Cell viability was determined in a trypan blue test. Typically, the cell suspension contained at least 95% viable lymphocytes.

At the same time, blood was taken from a finger to determine the total number of leukocytes and calculate the leukocyte formula, which was necessary for the subsequent determination of not only the relative, but also the absolute number of immunocompetent cells.

100 µl of a suspension of lymphocytes and the corresponding erythrocyte diagnosticum were poured into the wells of the plate for immunological reactions, the mixture was precipitated by centrifugation at 1000 rpm for 5 minutes and incubated for 60 minutes at +4°C. The reaction was stopped by adding an equal amount of glutaraldehyde (final concentration 0.06%, +4°C, 20 min). The contents of the wells were shaken out with a sharp movement, the wells were filled with distilled water and stored until the results were counted (from 2-3 days to 1 week). On the day of counting, the contents of the wells were shaken out, an equal amount (100 µl) of Zadorozhny-Dozmorov's dye was poured into the wells to stain the nuclei of lymphocytes, the cells were resuspended, the "crushed drop" preparation was pre-

pared, and the number of rosette-forming cells (ROCs) was counted in relation to free lymphocytes using magnification biological microscope 7×40. 200 lymphocytes were counted, ROCKs were isolated from them, then the average value was found in percent. A lymphocyte with 3 or more erythrocytes tightly attached to its surface was taken as ROCK.

Also in our studies, we used the method of paired sera, in which specific IgG and IgM are determined using the ELISA method. The principle of the method is that a double blood sampling is performed from the patient within 10-14 days. After that, these 2 samples are simultaneously examined under the same conditions for the presence of specific antibodies using ELISA. An increase or decrease in titers of specific immunoglobulins of the IgG and IgM class makes it possible to draw an appropriate conclusion and make a diagnosis.

: determination of interferon α and γ: the level of antiviral (α-IFN) and pro-inflammatory (γ-IFN) interferons in peripheral blood serum was studied by enzyme immunoassay using Vector-Best test systems (Novosibirsk, Russia).

The first monoclonal antibodies (mAbs) were preliminarily immobilized on the inner surfaces of the cells of collapsible microtiter plates. In each of the wells make the second mAb (to an independent epitope of the INF -α molecule), conjugated with biotin, in the amount of 50 µl per well (dilution of AT 1:10). In the first two vertical rows of microplate cells, 200 µl of standards are added: A-0 pg/ml IFN-α, A - 5 pg/ml, C - 10 pg/ml, D - 25 pg/ml, E - 50 pg/ml, F - 100 pg/ml, G - 250 pg / ml, H - 500 pg / ml. 200 µl of samples are added to the remaining wells. If the expected concentration of INF - α in the samples exceeds 500 pg/ml, then they are pre-diluted and this dilution is taken into account when determining the concentration. Samples (tested and standard) are incubated for 1.5 hours at +37 ºC in a dry-air thermostat with continuous shaking. After incubation, the solution is removed from the cells. The cells are washed three times by adding 300 µl of washing solution to each of them, removing it with a pipette or a vacuum pump. The in-

dicator mechanism in this assay is horseradish peroxidase avidin conjugate, which has a very high affinity for biotin, which is conjugated to the second mAbs used in the assay. 200 µl of avidin conjugate with horseradish peroxidase at a dilution of 1:100 is added to each cell, incubated with samples for 45 minutes at +370ºC in a dry-air thermostat with continuous shaking. The conjugate solution is removed from the wells. This is followed by washing and staining.

Determination of total IgE and allergen-specific IgE antibodies was also carried out by enzyme immunoassay (Ovsyannikova I. G. et al., 1985; Gervazieva V. B., 1987).

Determination of the level of cytokines. In the present work, to determine the level of cytokines in blood serum, we used enzyme-linked immunosorbent assays, which are the most widely used. These systems use multi-antibody kits. Monoclonal antibodies (mAbs) are used as the first antibodies, which are collected on 96-well plates and have the ability to capture an antigen (cytokine) from a solution. Biotinylated polyclonal antibodies (pAT), which are "opened" by the streptavidin-enzyme-substrate complex, were used as the second antibodies. It is also possible to use sets of three antibodies, when the second polyclonal antibodies are "opened" with anti-species antibodies conjugated with enzymes. The result is a "sandwich" of two or three antibodies and an antigen molecule between them. The results were quantified by comparing the results with the curve of dependence of the optical density of the solution on the concentration of the standard antigen. The linear section of the standard curve is used for the calculation.

ELISA methods are highly specific, fast (the time of ELISA is less than 5 hours) and relatively easy to perform. The sensitivity threshold for such test systems reaches 0.5 pg/ml.

Induction of cytokine synthesis. For the synthesis of cytokines, we used:

- laminar box or box room for sterile works
- flat-bottomed 96-well cell culture plates

- automatic pipettes with sterile tips (0-200 µl)

- spirit lamp

- cytokine inducers - PHA and prodigiosan

- CO_2 - an inductor or a thermostat at 37 C and the possibility of maintaining a 5% level of CO_2 for cell cultivation .

Determination of cytokines-mediators of intercellular interaction in the immune response and inflammation.

Determination of TNF - α, IL -1β, IL -4.

The first monoclonal antibodies (mAb) were preliminarily immobilized on the inner surfaces of the cells of solid plates for ELISA. In the first two vertical rows of cells of the plates, 100 µl of standards are added: A-0 pg/ml of the cytokine under study, B-50 pg/ml, C-250 pg/ml, D-500 pg/ml, E - 1000 pg/ml, F - 2000 pg / ml of cytokines. The rest of the cells contribute 100 pg/ml samples. Samples and standards contribute in the recommended buffers. The tablet is incubated for 1.5 hours at 18-20 °C. After incubation, the solution is removed from the cells using a pipette or a vacuum pump. The wells are then washed three times by adding 300 µl of washing solution to each of them. The rest of the washing solution is removed with a pipette or a vacuum pump. The second mAbs labeled with biotin are added in 100 µl and the samples are incubated with them for 1.5 hours with continuous shaking at 18 °C. After incubation, the solution is removed from the cells using a pipette or a vacuum pump. The wells are washed three times by adding 300 µl of washing solution to each of them. The rest of the washing solution is removed with a pipette or a vacuum pump. The conjugate of strepavidin with horseradish peroxidase diluted 1:100 with buffer is added in 100 µl to all plates and incubated at 18 °C with continuous shaking for an hour. After incubation, the solution is removed from the cells using a pipette or a vacuum pump. The indicator mechanism in this assay is a high affinity for biotin, which is conjugated to the second mAbs used in the assay. After that, the stages of washing and coloring are carried out.

2.2.5 Determination of the degree of bacterial contamination in children with acute stenosing laryngotracheitis

The microbiocenosis of the upper respiratory tract was determined using a - bacteriological study. To do this, the material was taken with a pre-crown swab, then placed in an enrichment medium (Eagle's medium or 199 Parker's medium). This was achieved by the accumulation of the pathogen in the cells of the epithelium of the mucous membrane of the posterior wall of the larynx, which significantly increases the probability of isolation of the pathogen. Inoculations in the accumulation medium were incubated at t - 37 ° C for 18-24 hours, then inoculation was carried out with a swab on nutrient media. Identification of isolated microorganisms was carried out in accordance with the tests recommended in the Burgey Bacteria Key .

Simultaneously with the cultures, a microscopy of a Gram-stained smear was performed. Along with inoculations under anaerobic conditions, ordinary inoculations were carried out under aerobic conditions on conventional media for the isolation of facultative microorganisms (Endo medium, 5% blood agar, sugar broth, yolk-salt medium) according to the standard method. Aerobic microbes were studied according to the standard method of M.O. Birger (1965), and anaerobic microflora according to the method of V.I. Kocherovets et al. (1986). Anaerobic microorganisms were identified using anaerodisks and by studying their biochemical activity.

The susceptibility of aerobic microbes was determined by diffusion from standard discs on a solid nutrient medium, and anaerobic microbes by diffusion in agar using discs with antibiotics under anaerobic conditions. The quantitative content of microorganisms in 1 ml of pathological material (exudate) was expressed in decimal logarithms of absolute numbers. In the presence of several representatives

of aerobic or anaerobic microbes, the total content of these groups of microbes was calculated by the sum of the geometric mean concentrations of the isolated representatives.

The dynamics of pathogen elimination was assessed by determining the degree of bacterial contamination in colony-forming units/g of tissue (Kuzin M. I., Kolker I. I., Kostyuchenok B. M. et al. 1980). The number of microbes in the 1 rtissue was calculated by the formula:

U = n · 10·10 (100 or 1000 depending on dilution)·K,

Where U - the number of microbes in the 1 rtissue, n - the number of colonies grown on the dish, 10 - recalculation per gram of suspension, 10 (100 or 1000) - dilution of the material inoculated on the dish, from which the colonies are counted, K - coefficient of recalculation of the sample for 1 rbiopsy.

Determination of the activity of saliva lysozyme was carried out according to the method of V.M. Shubika (1986 г.). The method is based on the determination of changes in the optical density of a standard live suspension Micrococcus lysodeikticus under the influence of lysozyme contained in saliva. The normative indicators of lysozyme range from 17 to 25%.

2.2.6. Biochemical research

All biochemical studies to determine the parameters of lipid peroxidation and AOZ were carried out at the Moscow Scientific Research Institute of TMA in the biochemical laboratory.

Determination of LPO processes in the blood serum by the level of MDA. The intensity of CL was studied according to the method of Yu. A. Vladimirov, A. I. Archakov (1972). Blood was collected from the cubital vein in the morning. 2.0 ml of 0.28% $CaCl_2$ solution and 0.04 ml of 1% heparin solution were added to 4.0 ml of blood , then the tube was gently shaken and left for 5 min at room tempera-

ture. The resulting suspension of erythrocytes was centrifuged for 10 min at 3000 rpm, after which the supernatant was removed, and 18.9 ml of phosphate buffer pH 7.45 (60.0 ml of KH_2PO_4 and 105 мMKS1) was added to the precipitate. The cuvette with the resulting suspension was placed in the measuring chamber of the KhLMTS-01 device (Russia) and the background values were recorded. To initiate CL, 0.1 ml of a 25 mm solution of divalent iron ($FeSO_4$-7 H_2O) was introduced using a dispenser . Immediately after the addition of iron, a rapid burst of chemiluminescence (h) occurs, which lasts for several seconds, its duration and intensity correspond to the concentration of lipid hydroperoxides. Then comes the latent period (τ), the duration of which depends on the ratio of pro- and a antioxidants in the system under study. The CL intensity was judged from the value of the light sum of a fast flash per unit time . The measurement of each test sample was carried out in two parallel studies, then the average value was derived. Chemiluminescence intensity was expressed in pulses per second (imp/s). It should be added that the necessary conditions for the passage of the reaction are constant stirring of the reaction mixture and a stationary solution temperature of 37°C.

Definition of MDA carried out according to the method of N. A. Andreeva et al. (1999). To 0.3 ml of erythrocyte membranes were added 3.0 ml of 1% phosphoric acid, 1.0 ml of 0.6% thiobarbituric acid (TBA) and 0.1 ml of iron sulfate solution (28 mg $FeSO_4$ 7 H_2O , dissolved in 10.0 ml of distilled water).

The test tubes with drop catchers were placed in a boiling water bath for 1 hour, then cooled in cold water, 4.0 ml of butanol was added, thoroughly mixed, and centrifuged for 10 min at 3000 rpm. The optical density (Eop) of the upper (- $_{butanol}$) phase was measured against butanol at a wavelength of 535 nm. The calculation of the content of products reacting with TBA was carried out taking into account the molar extinction coefficient of MDA, equal to $1.56\ 10^5$ mol cm $^{-1}$ according to the formula:

$$A = \frac{Eon \cdot 10^6 \cdot 4{,}0}{1{,}56 \cdot 10^5 \cdot 0{,}3} = Eon \cdot 85{,}47$$

where A is the MDA content (in nmol/l or nM/ml), 4.0 is the volume of the butanol phase (ml), 0.3 is the sample volume.

DC

SOD activity was determined according to the method of E. E. Dubinina et al. (1983).

To 2.0 ml of pre-hemolyzed and washed in saline at t =4 ^{0} With erythrocytes (or EBC) was added 0.6 ml of ethyl alcohol, 0.3 ml of chloroform and 600 mg of crystalline KH_2PO_4. Substances interfering with the determination of SOD activity were precipitated by stirring the solution with a glass rod, followed by centrifugation in 12000 ga K-24 centrifuge (Germany) at a temperature of 4 ^{0} C for 15 min. The resulting supernatant was added to the incubation mixture in an amount of 0.2 ml. The composition of the incubation mixture included 1 μM EDTA, 1 mg gelatin, 0,407 мMnitro blue tetrazolium (NBT), 1.8 μM phenazine metasulfate (PMS), 0.1 ml 1 мMNADH. NADH was dissolved in 1 MTris-EDTA, pH 8.0. The total volume of the incubation mixture was adjusted to 3.0 ml with phosphate buffer (0,15 M), pH 7.8. Incubation was carried out for 10 min in the dark at room temperature (20-22 ^{0}C) under aerobic conditions. After 10 min, the optical density of the samples under study was measured on an SF-46 spectrophotometer (Russia) at a wavelength of 540 nm against a mixture containing all components except NAD·H. To calculate the activity of SOD, we first determined the percentage of inhibition of the NBT reduction reaction in the experimental sample for 1 min (T%). It is generally accepted that 50% incubation of this reaction corresponds to one conventional unit of SOD activity. According to the formula A=T%/(100%-T%), the value of the activity of the enzyme introduced into the cuvette was calculated, which was expressed in arbitrary units calculated per 1.0 ml of the biological solution under study (U/ml).

The activity of QDs was assessed according to the method of M.A. Korolyuk et al. (1988).

To 0.1 ml of erythrocytes (EBC) was added 2.0 ml of 0.03% hydrogen peroxide solution (H_2O_2). In a blank sample, 0.1 ml of distilled water was added instead of plasma. The reaction was stopped after 10 minutes by adding 1.0 ml of 4% ammonium molybdate. The intensity of the developed color was measured on SF-46 at a wavelength of 410 nm against a control sample, in which 2.0 ml of water was added instead of hydrogen peroxide.

The QD activity was calculated by the formula:

A \u003d (Ehol-Eop) · *V* · *t* ·*k* (mkat / l),

where A is the activity of catalase (mkat/l), Exhol and Eop are the extinction of blank and experimental samples, V is the plasma volume (0.1 ml), t is the incubation time 600 s, k is the molar extinction coefficient $22.2 \cdot 10^{3}$ mm^{-1} cm^{-1}.

2.2.7. Determination of the degree of endogenous intoxication in children with acute stenosing laryngotracheitis

In order to diagnose the nature and severity of the intoxication syndrome, we a dynamic study of indicators was carried out: MSM - according to the method of N. I. Gabrielyan (1982), a toxic blood factor using specific antigenic biological tests - a paramecium test-determining the time of death of paramecium in the patient's blood serum (Pafomov V. V. et al., 1980), also determined circulating immune complexes - CEC (Haskova , 1978) and calculation of the leukocyte index of intoxication - LII (Kalf-Kalifa Ya. Ya., 1975).

The degree of endogenous intoxication of the body was assessed by the content of medium-weight molecules in the blood serum and by the Kalf-Kalif index (leukocyte intoxication index - LII), which was calculated by the formula:

$$ËÈÈ = \frac{(4Ì + 3Þ + 2Ï + Ñ)(Ïë + 1)}{(ëèìô. + ïîí.)(ý + 1)}$$

where: M - myelocytes; Yu, P and C - respectively young, stab and segmented neutrophils; Pl - plasma cells; L - lymphocytes; M-monocytes; E - eosinophils.

2.3. Assessment of the degree of immune disorders and the effectiveness of immunocorrection

The optimal number of patients in the group. To obtain reliable results, a clinical-immune study must be carried out by analyzing the optimal number of patients. To do this, a preliminary limited observation is carried out on a small number of patients (5-6 people in a group), traditional primary statistical processing of the data obtained is carried out, the average values of the parameters in the compared groups are calculated, and their standard deviation is determined. According to the formula L.E. Kholodov and V.P. Yakovleva approximately calculate the required number of patients in groups to obtain objective conclusions:

$$n = \frac{\left(\sigma_1^2 + \sigma_2^2\right)}{(M_1 - M_2)^2}$$

The values of M_1 and M_2 are the average values of the indicators in the group, σ_1 and σ_2 are the standard deviation.

When assessing the immune status, the parameters of the patient's immunogram are compared with the parameters of healthy people. Each laboratory should have its own control (norm) of people of the same age, one-time, but not professional donors, taking into account blood groups, the presence or absence of the Rh factor, the time of year of the study. When interpreting the data of the immune examination, it is necessary to take into account the dependence of changes in indicators on age, biological rhythms, etc. When analyzing the obtained data, one should take into account the existence of links between the level of immune reactivity and genetic markers of blood in a patient, for example, blood groups. The identification of these features in various diseases makes it possible to identify immunocompromised individuals without conducting an in-depth examination.

rating algorithm . Using the coefficient of diagnostic value or the magnitude of the degree of immune disorders, the studied parameters of the immune status are arranged in order of decreasing significance of differences from the given values. Summing up the degree of immune deficiency and hyperfunction of the immune system by the links of immunity, a conclusion is made about the suppression or stimulation of the immune status.

Frequency Analysis . The analysis of the average values of the indicators is inaccurate, because averages the variations in the parameters of individuals in a group, and they can be very different. The essence of frequency analysis is to determine the number of patients with indicators of a certain value (for example, the content of T-cells with the 2nd or 3rd degree of immune deficiency). This approach most accurately characterizes the disorders of the immune system in patients in the group.

Diagnostic value coefficient . Calculation of the coefficient of diagnostic value according to the formula of A. D. Gorelik and V. A. Skripkin (1974),

$K_j = \frac{2 \cdot (V_1^2 - V_2^2)}{M_1 - M_2}$, where

V_1, V_2 - the average value of the square deviation, M_1, M_2 - the average values of the indicators. Considering that the smaller the value K_j, the more this indicator differs from the norm, by selecting the three most significant parameters, it is possible to determine the formula for immune system disorders (Zemskov A. M., Zemskov V. M., 1993).

Calculation of the immune system disorders formula (FRIS) - using the coefficient of diagnostic value, which allows, taking into account the average values of the parameters and their dispersion, three leading parameters of the immune status were selected from all the studied parameters of the immune status, the most different from the normal level, indicating the direction (stimulation, decrease), degree immune disorders.

In patients with PSLT and RSLT, the effectiveness of complex therapy was additionally assessed by determining the indicated value according to the formula for stimulating immune parameters, taking into account the results of the therapy:

$$\frac{\%\ больных\ с\ 2-3\ СИН\ после}{\%\ больных\ с\ 2-3\ СИН\ до}\times 100\%$$

If the obtained value has a + sign and lies in the range from 1 to 33% - the first degree of stimulation, 34-66% - the second, more than 66% - the third.

$$SE=\frac{Рис-Рm}{Рис}-\frac{Рис-Рм}{Рис}\cdot 100\%$$

where *Fig* - the value of the parameter in absolute terms before the start of treatment; *RT* - parameter value after traditional therapy; *Pm* is the value of the parameter after traditional treatment with an immunomodulator.

2.4. Statistical processing of research results

The data obtained during the study were subjected to statistical processing on a Pentium-IV personal computer using the Microsoft Office Excel-2012 software package, including the use of built-in statistical processing functions. Methods of variational parametric and non-parametric statistics were used with the calculation of the arithmetic mean of the studied indicator (M), standard deviation (σ), standard error of the mean (m), relative values (frequency, %). Significance level $P<0.05$ was taken as statistically significant changes. Statistical significance for qualitative variables was calculated using the χ^2 test (chi-square) and z-test (Glantz C. , 1998) using the following formula:

$$z=(p_1-p_2)\sqrt{\frac{n_1\cdot n_2}{p(1-p)\cdot(n_1+n_2)}}$$

where $p_1 = \mu_1 / n_1$ and $p_2 = \mu_2 / n_2$ are compared experimental frequencies, and $p = (\mu_1 + \mu_2)/(n_1 + n_2)$ is the average frequency of occurrence of the trait in both groups.

CHAPTER III . FEATURES OF THE CLINICAL COURSE OF ACUTE STENOSING LARYNGOTRACHEITIS IN CHILDREN

3.1. Clinical and anamnestic features of the formation of primary and recurrent laryngotracheitis in children

Unfavorable course of ante-, intra - and neonatal periods and the presence of allergic reactions in early childhood are considered factors influencing the formation of a child's health.

Table 3.1 presents the results of the study of the characteristics of the medical and biological history. In the two studied groups, most of the mothers at the time of the birth of the child were aged 20 to 30 years (77.9% and 72.5%, respectively, in groups). Maternal health assessments showed that only 23 (15.0%) mothers whose children suffered from RSLT did not have chronic diseases, while this figure was 17 (13.9%) with PSLT.

Attention is drawn to the presence of chronic foci of infection (in group 1 - 48 (39.3%), in group 2 - 73 (47.7%)) and broncho-pulmonary diseases (in group 1 - 29 (23.8%) , in group 2 - 37 (24.2%)).

An analysis of hereditary history showed that a special place is occupied by the aggravation of his allergic (in group 1 - 49 (40.2%), in group 2 - 59 (38.6%)) and broncho-pulmonary diseases of relatives in the first and second line (in group 1 - 45 (36.9%), in group 2 - 62 (40.5%)).

The foregoing indicates a significant role of allergic reactions in the genesis of primary and recurrent forms of OSLT, and that the development of relapses is facilitated by hyperreactivity of the upper respiratory tract and the allergic mood of the child's body.

In our observations, there was no significant difference in the medical and biological history of the examined children with PSLT and RSLT.

Table 3.1

Peculiarities of Medical Biological History of Examined Mothers

Indicators	1 group (n=122)		group 2 (n=153)	
	abs	%	abs	%
Mother's age				
Up to 20 years old	17	13.9	23	15.0
20 to 30	95	77.9	111	72.5
Over 30	13	10.7	19	12.4
Maternal health				
Healthy	17	13.9	13	8.5
Broncho-pulmonary diseases	29	23.8	37	24.2
Cardiovascular diseases	9	7.4	7	4.6
Gastrointestinal tract	19	15.6	23	15.0
Chronic foci of infection	48	39.3	73	47.7
Burdening of hereditary anamnesis				
Not weighed down	9	7.4	12	7.8
allergic diseases	49	40.2	59	38.6
bronchopulmonary diseases	45	36.9	62	40.5
cardiovascular diseases	12	9.8	fifteen	9.8
oncological diseases	3	2.5	2	1.3
diabetes	four	3.3	3	2.0

Most of the mothers of the examined children (in group 1 - 63 (51.6%), in group 2 - 87 (56.9%)) are housewives. Occupational hazards at work of the mother are expressed in the dust content of the air in the workplace where they worked at the time of the birth of the child (in group 1 - 29 (23.8%), in group 2 - 43 (28.1%)). On the spot, increased nervous load at the place of work (in group 1 - 19 (15.6%), in group 2 - 13 (8.5%)). 48 (39.3%) children in group 1 and in group 2 - 47 (30.7%) are first-born (Table 3.2).

Table 3.2

Features of the anamnesis of mothers of the examined children

Indicators	1 group (n=122)	group 2 (n=153)

	abs	%	abs	%
Occupational hazards at mother's work				
None	63	51.6	87	56.9
weight lifting	0	0	7	4.6*
night shifts	9	7.4	3	2.0*
Air pollution	29	23.8	43	28.1
Poor resistance to stress	19	15.6	13	8.5
Number of pregnancies				
primigravida	48	39.3	47	30.7
Re-pregnant	74	60.7	106	69.3
Complications of a previous pregnancy				
Physiological course	eleven	9.0	17	11.1
Threat of interruption	31	25.4	41	26.8
Mild preeclampsia	19	15.6	23	15.0
Anemia	67	54.9	93	60.8

Note: * - differences relative to the data of group 1 are significant ($P < 0.05$)

Most women suffered from anemia (in group 1 - 67 (54.9%), in group 2 - 93 (60.8%)), and too few women with a physiological course of pregnancy (in group 1 - 11 (9.0%) , in group 2 - 17 (11.1%)). The threat of abortion was noted in 31 (25.4%) mothers of children in group 1 and in 41 (26.8%) - in group 2.

Slightly more than half of the women gave birth at term (in group 1 - 66 (54.1%), in group 2 - 83 (54.2%)), premature - (in group 1 - 39 (32.0%), in 2 group - 47 (30.7%)), post-term (in group 1 - 17 (13.9%), in group 2 - 23 (15.0%)). An analysis of the course of the birth of a real pregnancy showed that it was physiological only in 36.9% of cases in mothers of the 1st group and in 37.3% of the 2nd groups, but pathological births were observed in 63.1% of cases in mothers of the 1st group and in 62 .7% - 2 groups. A long waterless period was noted in 23 (18.9%) mothers of children in group 1 and in 5 (22.9%) - in group 2. The caesare-

an section was performed in 32 (26.2%) mothers of children in the 1st group and 43 (28.1%) in the 2nd group. Forceps were applied in group 1 - 3 (2.5%), in group 2 - 5 (3.3%), resuscitation - (in group 1 - 13 (10.7%), in group 2 - 17 (11.1%)). Chronic intrauterine hypoxia suffered in group 1 - 13 (10.7%), and in group 2 - 17 (11.1%) children (Table 3.3).

Table 3.3

Characteristics of the course of childbirth of a real pregnancy

Indicators	1 group (n=122)		group 2 (n=153)	
	abs	%	abs	%
childbirth				
On time	66	54.1	83	54.2
Premature	39	32.0	47	30.7
Overdue	17	13.9	23	15.0
The course of childbirth				
physiological	45	36.9	57	37.3
Pathological	77	63.1	96	62.7
Long dry period	23	18.9	35	22.9
C-section	32	26.2	43	28.1
Forceps delivery	3	2.5	5	3.3
Asphyxia during childbirth	13	10.7	17	11.1
Resuscitation measures	13	10.7	17	11.1
Prenatal dystrophy	39	32.0	47	30.7
Chronic intrauterine hypoxia	67	54.9	93	60.8

The neonatal period according to WHO is considered from the moment of birth to 27 days inclusive. In 45 (36.9%) children of group 1 and in 57 (37.3%) children of group 2, the neonatal period passed without complications and diseases. In other children, the neonatal period was complicated by infectious diseases and respiratory distress syndrome.

On the first day, the vast majority of children were attached to the mother's breast (in group 1 - 93 (76.2%), in group 2 - 105 (68.6%)). Mostly breast milk was received up to a year (in group 1 - 33 (27.0%), in group 2 - 53 (34.6%), more than a year - in group 1 29 (23.8%), in group 2 - 29 (19.0%) (Table 3.4).

Table 3.4

The course of the neonatal period

Indicators	1 group (n=122)		group 2 (n=153)	
	abs	%	abs	%
physiological	45	36.9	57	37.3
SARS, pneumonia and other infectious diseases	21	17.2	26	17.0
Purulent-septic diseases	17	13.9	23	15.0
Respiratory Disorder Syndrome	39	32.0	47	30.7
Attached to the chest				
On the first days	93	76.2	105	68.6
For 2-3 days	22	18.0	37	24.2
Later 3 days	7	5.7	eleven	7.2
duration of breastfeeding				
Up to 1 month	13	10.7	21	13.7
up to 6 months	38	31.1	29	19.0*
Up to 1 year	33	27.0	53	34.6
More than 1 year	29	23.8	29	19.0
Artificers	9	7.4	21	13.7

Note: * - differences relative to the data of group 1 are significant ($P < 0.05$)

The prevailing conditions in the development of acute laryngotracheitis that create an unfavorable premorbid background are: maternal health , heredity aggravation, occupational hazards at the mother’s work , complications of a previous - pregnancy, anemia, aggravated obstetric and gynecological anamnesis, pathological childbirth, prematurity, artificial feeding, complication of the neonatal period with infectious diseases and respiratory distress syndrome.

3.2. Etiological factors of primary and recurrent stenosing laryngotracheitis in children

In the existing pediatric and infectious practice, the concept that laryngotracheitis is considered a syndrome that more often appears in acute viral infections of various etiologies has developed and strengthened [Abdullaeva N.N., Tadzhibaev G.A., 2014; Alenina T. M., Karavaev V. E., Orlova S. N., 2002; Britkova T.A., Lekomtseva O.I., Yuzefovich N.V., Petrakova I.A., Guskov A.P., 2008; Mironov A. Yu., Savitskaya K. I., Vorobyov A. A., 2001].

Laryngotracheitis develops mainly against the background of acute respiratory viral infections (influenza, para influenza, adenovirus, PC infection), as well as with a mixed viral and bacterial etiology of diseases of the upper respiratory tract (Table 3.5).

Table 3.5

Etiological factors in the development of OSLT in children

Indicators	1 group (n=122)		group 2 (n=153)	
	abs	%	abs	%
flu	54	44.3	108	70.6***
parainfluenza	eight	6.6	eight	5.2
RS virus	eleven	9.0	6	3.9
Adenovirus	26	21.3	22	14.4
Viral-bacterial etiology	23	18.9	9	5.9***

Note: *** - differences relative to the data of group 1 are significant (P < 0.0 01)

It was noted that OSLT occurs more often with influenza: in group 1, 54 (44.3%) children with PSLT, and in group 2, 108 (70.6%) (P <0.001) children with RSLT developed relapses. With viral-bacterial etiology, a different picture is

observed: in group 1, 23 (18.9%) children and 9 (5.9%) (P <0.001), i.e. children develop PSLT more often than children of the 2nd group with RSLT.

When examining the anamnesis, it was found that in sick children, RSLT occurred against an unfavorable allergic background in 94.8% of cases. While a history of PSLT was detected in sick children, only 33.6% of patients had allergies (Table 3.6).

Table 3.6

Allergic diseases in examined children with ASLT

Diseases	1 group (n=122)		group 2 (n=153)	
	abs	%	abs	%
food allergy	7	5.7	37	24.2***
Conjunctivitis	3	2.5	eight	5.2
Rhinitis	eight	6.6	39	25.5***
Hives	5	4.1	16	10.5*
hay fever	four	3.3	9	5.9
Atopic dermatitis	6	4.9	21	13.7**
drug allergy	eight	6.6	29	19.0**
Quincke's edema	0	0	3	2.0

Note: * - differences relative to the data of group 1 are significant (* - P < 0.05, ** - P < 0.01, *** - P < 0.001)

In patients with recurrent ASLT, allergic diseases were significantly more common: urticaria (16 (10.5%) (P<0.001)), atopic dermatitis (21 (13.7%) (P<0.01)), drug-induced allergy (29 (19.0%) (P<0.01)) allergic rhinitis (39 (25.5%) (P<0.001), food allergy (37 (24.2%) P<0.001), atopic dermatitis matitis (21 (13.7%) P<0.01)). This indicates the importance of the allergic component in the development of diseases.

The seasonality of the disease is traced, exacerbations are observed more often in winter, autumn, autumn-winter periods. Moreover, the number of exacerbations in children with RSLT is observed more often than in other periods. The ex-

ternal environment (climatic features), as well as seasonality and environmental factors, play a leading role in the pathogenesis of OCLT (Table 3.7).

Table 3.7

Seasonality of the disease in examined children with ASLT

Seasons	1 group (n =122)		group 2 (n =153)	
	abs	%	abs	%
Winter	twenty	16.4	31	20.3
Spring	fifteen	12.3	eighteen	11.8
Winter-spring	16	13.1	19	12.4
summer	9	7.4	6	3.9
Autumn	27	22.1	36	23.5
autumn-winter	31	25.4	38	24.8
No seasonality	four	3.3	5	3.3

We have proved as a result of the analysis that the above etiological factors create conditions for the development of OSLT. These include: SARS, allergic diseases and seasonality.

3.3. Features of the formation of acute stenosing laryngotracheitis in children, taking into account the respiratory history of the first years of life

The first episode of laryngeal stenosis is usually observed in children in the age range from 1 to 5 years (Table 3.8).

Significant differences were found in children with RSLT compared with PSLT, which consisted in the fact that the symptoms of the disease in children with RSLT were more pronounced and repeated relapses were noted.

Primary SLT was observed in 26 (21.3%) under the age of 1 year, from 1 to 3 years - in 53 (43.4%), from 3 to 5 years - in 43 (35.2%) (Table. 3.8).

Table 3.8

Features of the formation of primary SLT depending on age

Age at which child first had SLT	Amount of children	
	abs	%
Up to 1 year	26	21.3
From 1 year to 3 years	53	43.4
3 to 5 years	43	35.2

37 (24.2%) children with RSLT underwent SLT for the first time at the age of 1 year, in the period from 1 to 3 years - 64 (41.8%), from up to 6 years - 52 (34.0%).

Once a year, a relapse was observed in 39 (25.5%), in 8 (5.2%) - 1 time in a year and a half, most often - 82 (53.6%) - 3 times a year and more often 3 times a year. year at 24 (15.7%).

Analysis of the length of time between the first and repeated SLT showed that after 1 month in 18 (11.8%) cases there was a relapse, in 19 (12.4%) - after 2-4 months. The overwhelming number of relapses recurred after 4-8 months in 27 (17.6%) cases and after 1-2 years - in (19.0%), and more than 2 years - in 42

(27.5%) cases. During the period between first and repeated cases of SLT in 46 (30.1%) children no viral and bacterial infection was observed infections , u 20 (13.1%) patients - 1 case of ARVI, at 2 2 (14.4%) patients - 2 cases, at 3 8 (24.8 %) - from 3 up to 5 and 27 (17.6 %) - more than 5 cases of acute respiratory viral infections, i.e. 42.7 % of children had three or more acute respiratory viral infections between the first and repeated SLT (Table 3.9).

Table 3.9
of RSLT depending on age, respiratory history of the first years of life, the frequency of relapses

Indicators	Amount of children	
	abs	%
Age at which child first had SLT:		
- up to 1 year	37	24.2
- from 1 to 3 years	64	41.8
- 3 to 5 years	52	34.0
Number of relapses:		
- less than once a year	eight	5.2
- 1 time per year	39	25.5
- 3 times a year	82	53.6
- more than 3 times a year	24	15.7
Time interval between the first and repeated OSLT:		
- 1 month	eighteen	11.8
- 2-4 months	19	12.4
- 4-8 months	27	17.6
- 8-12 months	eighteen	11.8
- 1-2 years	29	19.0
- more than 2 years	42	27.5
Illness between first and second SLT		
- SARS - 1 case	twenty	13.1

- SARS - 2 cases	22	14.4
- SARS - from 3 to 5 cases	38	24.8
- SARS - more than 5 cases	27	17.6
- no illnesses	46	30.1

According to the clinical examination of children, many of them admitted to the laryngitis department during the acute period of ASLT had an increase in body temperature in children with PSLT 79 (64.8 %) hospitalized, and with RSLT - in 51 (33.3 %), arrhythmic syndrome in the form of conjunctivitis, nasal congestion, nasopharyngitis was observed in 96 (75.2%) children with recurrent SLT (P <0.001) and in 103 (84.4 %) - with primary (Table 3.10).

The nature of the cough in the majority of those admitted was "barking", (109 (89.3%) and 146 (95.4%), respectively, in groups), almost all of them had hoarseness or hoarseness, various wheezing wheezes in children with RSLT 3.5 times more than in children with PSLT.

Table 3.10

Data from an objective examination of children with ASLT

Symptoms	1 group (n=122)		group 2 (n=153)	
	abs	%	abs	%
Hoarseness or hoarseness	122	100.0	153	100.0
catarrhal syndrome	103	84.4	96	62.7***
Rough barking cough	109	89.3	146	95.4
Rough, wet cough	13	10.7	78	51.0***
Breathing silent	64	52.5	29	19.0***
Heat	79	64.8	51	33.3***
No changes in the lungs	64	52.5	27	17.6***
Dry wheezing	48	39.8	21	13.7***
Various moist rales	ten	8.2	35	22.9***

Note: * - differences relative to the data of group 1 are significant (* - P < 0.05, ** - P < 0.01, *** - P < 0.001)

Physical examination in the lungs during RSLT revealed no changes in 27 (17.6 %) children , 21 (13.7 %) children had dry wheezing rales, 35 (22.9 %) children had mixed wet rales (P <0.001) . During PSLT, auscultatory changes in the lungs were not observed in 27 (17.6 %) children , dry wheezing rales were detected in 48 (39.8 %) children , wet rales of various sizes - also in 10 (8.2 %) children .

An analysis of the frequency of symptoms of respiratory failure in the examined children showed that they occur much more often in children with RSLT than in children with PSLT, which indicates their weakened condition (Table 3.11).

Table 3.11

The frequency of symptoms of respiratory failure in the examined children

Symptoms	1 group (n=122)		group 2 (n=153)	
	abs	%	abs	%
inspiratory dyspnea	81	66.4	129	84.3***
Paleness of the skin	98	80.3	107	69.9*
Cyanosis of the nasolabial - triangle	73	59.8	117	76.5**
acrocyanosis	17	13.9	21	13.7
General cyanosis	9	7.4	22	14.4
Tachycardia	79	64.8	51	33.3**
bloat wings of the nose	60	49.2	137	89.5***
Neck muscle tension	73	59.8	103	67.3
Participation in the act of breathing intercostal muscles	53	43.4	104	68.0***

Note: * - differences relative to the data of group 1 are significant (* - P < 0.05, ** - P < 0.01, *** - P < 0.001)

inspiratory shortness of breath in children with RSLT by 79.3%, (P <0.001) , noisy breathing - 2.1 times, for the collapse of the pliable places of the chest - 2.9

times more often than in children with PSLT. The duration of laryngeal stenosis was up to 1 day - 88 (57.5 %) with RSLT , up to 3 days - 51 (33.6 %) , more than 3 days - 15 (9.8 %) ; with PSLT, respectively , 50 (4-1 %) , 56 (45.9 %) , 16 (13.1 %) (Table 3.12) .

Table 3. 12

Symptoms of stenosis and its duration in examined children

Symptoms	1 group (n=122)		group 2 (n=153)	
	abs	%	abs	%
Symptoms of stenosis				
Inspiratory dyspnea	81	66.4	129	84.3***
Vesicular respiration	58	47.5	124	81.0***
Retraction of pliable places of the chest	27	22.1	79	51.6***
Duration of laryngeal stenosis				
Up to a day	fifty	41.0	88	57.5**
From 1 to 3 days	56	45.9	51	33.6*
More than 3 days	16	13.1	fifteen	9.8

Note: * - differences relative to the data of group 1 are significant (* - P < 0.05, ** - P < 0.01, *** - P < 0.001)

When assessing the severity of OSLT by degrees, we considered three - components:

- hoarseness or hoarseness and barking cough ;

- symptoms of stenosis: inspiratory dyspnea, noisy breathing, retraction of compliant chest areas;

- respiratory failure: inspiratory shortness of breath, pallor of the skin, cyanosis of the nasolabial triangle , tachycardia, participation of accessory muscles in the act of breathing (swelling of the wings of the nose, participation in the act of breathing of the intercostal muscles).

The severity of croup syndrome in the children we observed was established on the basis of clinical symptoms :

OSLT I degree was observed in 30 (24.6%) children with PSLT and in 26 (17.0%) - RSLT.

II degree was observed in 80 (65.6%) children with PSLT and in 104 (68.0%) children with RSLT, the general anxiety of the patient.

III degree stenosis was observed in 12 (9.8%) children with PSLT and in 23 (15.0%) children with RSLT.

At the IV degree of stenosis, a sphyxia occurs. At present, it is practically not found. None of the children we observed had it (Table 3.13).

The vast majority of patients were admitted to the infectious diseases hospital no 3 г. Tashkent to the laryngitis department with the II degree OSLT clinic. The development of stenosis up to the III degree was noted only in isolated cases , only in children with a recurrent course of the disease.

In patients with ASLT symptoms were observed intoxication: fever, headache , weakness, loss of appetite. We have revealed a significant difference in the manifestation of intoxication syndrome in the groups of patients with OSLT and RSLT.

Table 3.13

Distribution of the examined children according to the severity of OSLT

Degrees stenosis	1 group (n =122)		group 2 (n = 153)	
	abs	%	abs	%
I degree	thirty	24.6	26	17.0
II degree	80	65.6	104	68.0
III degree	12	9.8	23	15.0
IV degree	0	0	0	0

All the children observed by us had OSLT symptoms, such as: hoarseness, hoarseness, up to aphonia, as well as a rough barking cough.

Thus, the analysis of the premorbid background of children suffering from ASLT makes it possible to identify the main risk factors for the development of

the disease: repeated acute respiratory viral infections, allergic diseases, aggravated hereditary, obstetric anamnesis.

3. 4. Activity of pro- and antioxidant systems in erythrocyte membranes in children with primary and recurrent laryngotracheitis

The main link in the pathogenesis of functional changes in organs and systems during OSLT in children is the development of respiratory failure, manifested by a disorder of external, pulmonary and tissue respiration, hypoxia and hypoxemia. Under the influence of hypoxia and hypercapnia, the functional state of the central nervous system and the neuro-reflex regulation of the vital functions of the body are disturbed. As a result of impaired functions of the most important organs and systems in the body, changes in metabolism occur. Violation of gas exchange and redox processes, hypoxia and hypoxemia lead to the activation of anaerobic oxidation of underoxidized metabolic products. Under the influence of hypoxia, bacterial toxins, products of impaired metabolism and changes in hemodynamics in children with OSLT, there are violations of the function of vital organs. These changes are accompanied by an increase in the activity of LPO processes and a restructuring of the antioxidant defense systems of erythrocytes.

In this work, a study was conducted to determine the level of lipid peroxidation - by the initial product of DC in erythrocyte membranes and the final product of lipid peroxidation - MDA.

The study revealed an increase in the intensity of free radical processes against the background of a progressive insufficiency of antioxidant systems in the lymphocytes of children with OSLT, a deepening of the manifestations of immunodeficiency in the T-link. During the period of exacerbation of the disease, there is a significant increase in the level of MDA in patients of group 1 to 2.79 ± 0.11 nmol / l, in group 2 - 8.23 ± 1.11, which exceeds the control by 2.33 times and 2.9

times respectively, by groups, and DC reaches the level in patients of the 1st group up to 3.27±0.09 U/ml, in the 2nd group - 5.61±0.69. The results obtained indicate a significant activation of LPO processes. The level of SOD decreased in group 1 by 99.5%, in group 2 - by 99.6%, which indicates structural and functional changes in the lymphocyte membrane.

Activation of lipid peroxidation and AOS, as a result of this, the presence of changes in the lipid structure are the basis for the implementation of therapeutic and preventive measures aimed at correcting these disorders.

Table 3.14

Activity of pro- and antioxidant systems in erythrocyte membranes in children with PSLT and RSLT

	Indicators	Control group (n= 40)	1 group (n=122)	group 2 (n=153)
FLOOR	MDA, nmol/l	2.79±0.11	6.51±0.22***	8.23±1.11***
	DC, U/ml	1.43±0.02	3.27±0.09***	5.61±0.69***
AOZ	SOD, U/ml	2.41±0.09	1.21±0.01***	1.01±0.01***
	RT, μmol/mg	11.55±0.77	7.96±0.31***	5.66±0.39***

Note: * - differences relative to the data of the control group are significant (* - P < 0.05, ** - P < 0.01, *** - P < 0.001)

Thus, the conducted studies have established a significant pathogenetic role of antioxidant dysfunction in the body during OSLT in children. Changes in the LPO-AOD system are the leading mechanism of dysfunction of lymphocytes. The loss of functional activity of immunocompetent cells during OSLT can be associated with an imbalance of the oxidant and antioxidant systems. Analysis of new data on the pathogenesis of OSLT allows us to conclude that a significant and long-term increase in the intensity of LPO is the most important mechanism for the formation of OSLT, reduces the functional activity of lymphocytes, causes the formation of immunodeficiency and, as a result, a severe course of the disease.

3.5. Endogenous intoxication syndrome in children and its impact on the clinical course of various forms of TB

In the pathogenesis of OSLT in children, one of the leading clinical manifestations is the syndrome of endogenous intoxication. These are, first of all, destructive processes, as a result of which an excessive amount of intermediate and final metabolic products accumulate in the body, which have a toxic effect on the most important life support systems. It is important to study the degree of endotoxemia and its influence on the clinical course of OSLT.

As shown by the results of laboratory studies in patients with OSLT at the height of clinical manifestations, there was a significant increase in the content of all indicators of endogenous intoxication in comparison with the healthy group. So, for example, SMP in children with PSLT increased by 94.6% and in children with RSLT - by 114.6%, the toxic factor in children with PSLT increased by 81.5% and in children with RSLT - by 134.7% (Table 3.15).

Table 3.15

Indicators of endotoxemia in children with ASLT

Indicators endotoxemia	Control group (n =40)	1 group (n =122)	group 2 (n=153)
SMP, arb. unit	0.280±0.04	0.545 ±0.05***	0.601 ±0.05***
TF, c.u.	26.5±1.36	48.1 ±1.1***	62.2 ± 5.9 ***
CEC, arb. unit	52.1 ±5.9	175.0 ±10.1 ***	216±14.8***
LII, conventional units	0.23±0.04	1.01±0.01 ***	1.7±0.04***

Note: * - differences relative to the data of the healthy group are significant (* - P <0.05, ** - P <0.01, *** - P <0.001);

The CEC level in children with PSLT increased by 3.4 times, and in children with RSLT by 4.1 times. Consequently, the level of the CIC in children with OSLT was combined with the severity of the patient's condition. Comparing the informativity of indicators in the assessment of EI, it should be noted that the most informative was LII , the level of which in children with PSLT increased by 4.4 times, and in children with RSLT - by 7.4 times.

It should be noted that when comparing the indicators of the content of EI - SMP, TF, CEC and LII with clinical symptoms of intoxication, the highest values were recorded in patients with a very serious condition, the higher the level of indicators of the content of EI, the higher the degree of intoxication.

Thus, our studies revealed an increase in the CEC, which, as is known, play a direct role in the pathogenesis of bacterial infections.

Analyzing the data presented in Table 3.16, it can be judged that with OSLT in children, the level of indicators of endogenous intoxication is in direct proportion to the clinical features and severity of the course.

In moderate condition, the level of SMP increased by 14.7%, in severe condition - by 94.6%, and in very severe condition - by 141.1% in relation to the corresponding indicator of healthy children (Table 3.16).

Table 3.16

Indicators of endotoxemia in children with PSLT by severity

Degree of intox-ication	SMP, c.u.	TF, c.e.	CEC, c.u.	LII, units
Healthy	0.280±0.04	26.5±1.36	52.1 ±5.9	0.23 ± 0.04
Medium-heavy	0.321 ±0.05**	33.5 ±1.8***	82 ±3.1***	0.42± 0.05 **
heavy	0.545 ±0.05***	48.1 ±1.1***	175.0 ±10.1 ***	1.01±0.01 ***
Highly heavy	0.675±0.06***	53.9 ± 2.7 ***	228.0±3.6***	2.61 ±0.02 ***

Note: * - differences relative to the data of the healthy group are significant (* - P <0.05, ** - P <0.01, *** - P <0.001)

In a moderate condition, the level of the toxic factor increased by 26.4%, in a severe condition - by 81.5%, and in a very severe condition - by 103.1% in relation to the corresponding indicator of healthy children.

An almost identical picture is emerging in children with RSLT, it is noted that the level of indicators of endogenous intoxication is in direct proportion to the severity of the course of the disease, only the level of indicators is much higher than in children with PSLT (Table 3.17).

Table 3.17

Indicators of endotoxemia in children with RSLT by severity

Degree intoxication	SMP, c.u.	TF, c.e.	CEC, c.u.	LII, units
Healthy	0.280±0.04	26.5±1.36	52.1 ±5.9	0.23 ± 0.04
Moderate	0.490 ±0.05**	44.5 ±2.9***	130 ±15.4***	0.5± 0.08 **
heavy	0.601 ±0.05***	61.2 ±1.9***	216±14.8***	1.73±0.04 ***
very heavy	0.703±0.06***	75.9 ± 3.8 ***	306±17.6***	3.32 ±0.2 ***

Note: * - differences relative to the data of the healthy group are significant (* - P <0.05, ** - P <0.01, *** - P <0.001)

In conclusion, I would like to note that the risk factors for the occurrence and development of ASLT in children are: burdened heredity, male gender, early age of the child, frequent respiratory allergic diseases, as well as a burdened allergic anamnesis, in which maternal allergy is of particular importance .

The problem of combating SEI is very relevant, since this syndrome occurs in almost all children with critical conditions and is the leading one in the pathogenesis of OSLT. During OSLT, patients with depletion of reparative processes and a sharp decrease in the natural functions of the body may develop an infectious-toxic shock. Its development is due to the use of large doses of antibiotics, since this causes the death of a large number of pathogens and an abundant intake of endotoxins into the blood, in which the serious condition of the body is aggravated by a sharp violation of hemodynamics, circulation and perfusion of tissues. In the pathogenesis of shock, the leading place is occupied by a violation of micro- and macrocirculation. It is high EI in these conditions that is the main factor of lethality.

CHAPTER IV . CLINICAL AND IMMUNOLOGICAL CHARACTERISTICS
CHILDREN WITH PRIMARY AND RECURRENT LARYNGOTRACHEITIS

In the development of acute stenosing laryngotracheitis, factors of the - immune defense of the body play an important role. Literature data indicate that OSLT reveals significant changes in the cellular link of immunity, which are expressed in a decrease in the total content of T-lymphocytes. The state of humoral immunity is characterized by disimmunoglobulinemia . At the same time, most researchers note a decrease in IgA and IgG in combination with an increased level of IgM. A downward trend in IgM occurs mainly in uncomplicated ASLT [Burton D. _ M. , Seid A. _ B. , Kearns D. _ B. , 2002; De soto H. , 2008; Williams J. _ V. , Harris P. _ A. , Tollefson S. _ J. , 2014].

In the occurrence of OSLT, the negative influence of individual peri- and postnatal factors matters. A complex of factors such as pneumopathy, including artificial lung ventilation (ALV) in the early neonatal period, severe forms of perinatal lesions of the central nervous system (CNS), the presence of thymomegaly, which reduce the effectiveness of adaptive reactions, predisposed to the development of OSLT in infancy and early childhood [Bjornson C. _ L. , Classen T. _ P. , Williamson J. , 2004; De soto H. , 2008; Wyatt J. , 2012].

The problem of RSLT in children is due to the increase in the incidence of diseases and the lack of a unified approach to the management of such patients. The immune status of patients with RSLT is characterized by a decrease in gamma globulins, as well as a significant decrease in IgA and IgA, an increased level of total IgE, but this pattern is not observed in all cases.

4.1 . Restructuring of cellular and humoral immunity in children with primary and recurrent laryngotracheitis

In clinical practice, usually based on the study of the main populations of immunocompetent cells (CD 3 - T-lymphocytes, CD 4 - T-helpers, CD 8 - T-suppressors and CD 20 - B-lymphocytes, NK cells, etc.) of the patient a conclusion is given on the state of cellular immunity. In addition, the immunoregulatory index (IRI) is taken into account - the ratio of CD 4 / CD 8. Based on the indicators (T-helpers and T-suppressors), one can judge in which of the two immunoregulatory populations deeper changes occur. However, these indicators reflect only quantitative changes in the T- and B-links of immunity. Our results show that the absolute number of leukocytes and lymphocytes in the peripheral blood of patients of both groups increased statistically significantly ($P<0.001$). Thus, in sick children with primary and recurrent laryngotracheitis, the number of leukocytes increased by an average of 65.8%, and the number of lymphocytes increased by 78.2%.

The most significant dynamics of changes was observed in patients of the 2nd group with RSLT, in whom the number of leukocytes increased by 2 times. This is approximately one third higher than the studied indicators of the 1st group of patients with PSLT. This implies that the presence of leukocytosis and lymphocytosis in the acute period confirms the development of the inflammatory process in the body.

An important link in the regulation of the immune system is the interaction of T- and B-class lymphocytes and their subpopulations. From the data in Table 4.1, it is obvious that the pathological process in PSLT and RSLT was accompanied by compensatory stimulation of the cellular mechanisms of the immune system. Since the absolute number of total T-lymphocytes significantly increased by 1.3 times with PSLT and 1.7 times with RSLT, there was also a significant increase in the percentage of T-lymphocytes in both groups.

As can be seen from the analysis of the obtained results, there is a significant increase in T-helpers ($P<0.001$) in patients with PSLT, and with RSLT it did not differ much from the control values.

In addition, the absolute number of T-suppressors, as well as their percentage, was statistically significantly increased in patients of group 1 (P<0.001), and in patients of group 2 it decreased compared to control values.

With PSLT and RSLT, IRI increased by 1.6 and 1.9 times, respectively, which indicates the development of autoimmune processes in the body

Table 4.1

Indicators of T-cell immunity in children with OSLT

Indicators	Control group (n= 30)	1 group (n=122)	2 group (n=153)
Leukocytes, (g/l)	7080 ±216.9	9 5 4 6 ±197.2***	8210 ±117.4*** ^^^
Lymphocytes, %	32.9 ±0.80	55.2 ±1.14***	57.0 ±0.86***
Lymphocytes, abs.	2344 ±104.6	5233 ±144.3***	4697 ±102.9*** ^^
CD3, %	60.9 ±1.82	61.7 ±1.28	66.3 ±0.86
CD3, abs.	1425 ±80.1	3241 ±114.6***	2920 ±75.0*** ^
CD4, %	38.7 ±1.09	35.1 ±0.77**	36.6 ±0.49
CD4, abs.	897 ±42.7	1838 ±66.5***	1726 ±46.3***
CD8, %	33.3 ±0.94	23.2 ±0.50***	21.5 ±0.31*** ^^
CD8, abs.	778 ±40.5	1214 ±43.7***	1006 ±25.4*** ^^^
CD4 / $_{CD8}$ _	1.20 ±0.05	1.61 ±0.05***	1.75 ±0.03*** ^
CD16, %	14.1 ±0.37	11.2 ±0.23***	9.9 ±0.13*** ^^^
CD16, abs.	333 ±18.3	592 ±22.5***	466 ±12.3*** ^^^

Note: * - differences relative to the data of the control group are significant (** - P <0.01, *** - P <0.001); ^ - differences relative to the data of group 1 are significant (^ - P <0.05, ^^ - P <0.01, ^^^ - P <0.001)

A disturbed balance of T-helpers and T-suppressors was revealed, which was accompanied by a sharp stimulation of the helper subpopulation in both forms, and against this background, there was a significant increase in T-suppressors in OSLT and a decrease in RSLT.

When assessing changes in the humoral link of immunity in patients with OSLT, a significant increase in B-lymphocytes was revealed compared to control

values by 1.3 times with PSLT and 1.5 times with RSLT. A similar picture was observed in percentage terms in both groups.

One of the most significant characteristics of the B-system of immunity is the concentration of serum immunoglobulins.

We have found that during OSLT, the content of immunoglobulin A in the blood is increased (2.0-2.9 times higher than normal values), which prevails in the composition of immune complexes.

Table 4.2

Indicators of the humoral link of immunity in children with ASLT

Indicators	Control group (n= 30)	1 group (n=122)	2 group (n=153)
IgA, ng/ml	179 ±5.4	107 ±2.1***	67 ±1.0*** ^^^
IgG, ng/ml	1221 ±38.0	778 ±16.0***	936 ±14.0*** ^^^
IgM, ng/ml	120 ±3.2	94 ±1.9***	102 ±1.4*** ^^^

Note: * - differences relative to the data of the control group are significant (*** - P <0.001); ^ - differences relative to the data of group 1 are significant (^ - P <0.05, ^^^ - P <0.001)

It is known that a full-fledged immune response of the body is provided by the cooperation of T- and B-lymphocytes. In this regard, it should be noted that the violations we identified indicate a violation of the cooperation of immunocompetent cells.

Changes in immunological parameters in patients with OSLT are associated with dysregulation of immunogenesis. To date, issues remain under-researched. functional state of the immune system in this category of patients. The study of these issues is of both scientific and practical interest, as it has the ultimate goal of not only discovering certain patterns in the development of the immune system in children with ASLT, but also a differentiated approach to their treatment in terms of increasing efficiency.

4.2. Assessment of the degree of disorders of the immune system

Since immunological indicators are very labile, there may be cases when they can differ significantly from the norm, but at the same time be adequate to the patient's condition (past or chronic infection, concomitant diseases, etc.).

Therefore, the assessment of hemo- and immunograms should be carried out taking into account the clinical picture and the calculation of the degree of immune disorders according to the formula (Zemskov A. M., 1995):

If the received answer has a "minus" sign, the patients are diagnosed with immune deficiency, while receiving a response with a "plus" sign - hyperfunction of the corresponding link of immunity. The results obtained also indicate the degree of immune disorder:

1 degree - 1-33% (does not require immunocorrection),

2 degree - 34-66%,

Grade 3 - more than 66% (grades 2 and 3 require mandatory immunocorrection).

The most informative indicator is the concentration of T-lymphocytes of various subpopulations, primarily T-helpers (C D 4) and T-suppressors (C D 8), as well as the IRI coefficient (the more severe the disorder, the lower it is).

For a more detailed assessment of immune disorders, the degree of immunological disorders was assessed using the formula of A. M. Zemskov and the method of frequency analysis, which characterizes the percentage of patients with significant changes (2-3 degrees) for each parameter under study.

According to the results of the frequency analysis in sick children of the 1st group, a decrease in both leukocytes in 20.0% and lymphocytes - in 23.0% at the level of the first degree was revealed. The amount of C D 4 was reduced within the

first degree in 37.0% of the subjects, which is a transient condition in this category of patients. Level C D 8 1 degree was observed in 56% and 44% - 2 degrees.

The study of immunoglobulins revealed a significant decrease in IgM within 1 degree in 55% and IgG - in 48% of patients. There was a transient deficiency of immunoglobulins A in 68%

A hyperfunction of T-lymphocytes III degree was observed in 47% of patients. The level of CD 3 increased to the level III degree in 47%.

Among immunoglobulins, the greatest increase in IgA was noted , its level reached grade II in 68%.

In sick children with PSLT, additional information is provided by building a rating of parameter changes based on the coefficient of diagnostic value, on the basis of which the formula for immune system disorders (ISD) was determined, which makes it possible to identify key indicators of hypo- and hyperfunction of the immune system by immunity: IgA_{2}^{-} IgM_{1}^{+} $CD8_{1}^{-}$ IgG_{1}^{-} $CD16_{1}^{+}$ $CD3_{1}^{+}$ $Lymph_{3}^{-}$ $CD4_{3}^{+}$ $Lake_{2}^{+}$ characterizing the presence of an imbalance in the immune system in patients with this condition (Table 4.3).

Analysis of the degree of violations of the immune status of sick children with RSLT according to the results of frequency analysis shows that a decrease in the number of leukocytes was observed in 20% of children, and an increase in 46% and both - 1 degree, which indicates that the number of leukocytes in 72% fluctuated within the normal range .

Table 4.3

The degree of violations of the immune status of sick children with PSLT according to the results of frequency analysis

Indicators	The degree of immune disorders (SIR)					
	immune deficiency			Hyperfunction of the immune system		
	I degree (%)	II degree (%)	III degree (%)	I degree (%)	II degree (%)	III degree (%)

Leukocytes	twenty	0	0	28	34	eighteen
Lymph.%	23	thirty	47	0	0	0
CD3, %	39	7	0	47	7	0
CD4, %	37	21	0	42	0	0
CD8, %	56	44	0	0	0	0
IRI	twenty	5	0	34	17	24
CD16, %	ten	0	0	22	21	47
IgA	32	68	0	0	0	0
IgG	48	52	0	0	0	0
IgM	55	29	0	16	0	0

And in 56% of children hyperfunction of the 3rd degree was observed. The number of lymphocytes increases: 11% have grade 1, 33% have grade 2, and 56% have grade 3 hyperfunction. 39% have CD3 immune deficiency - 1 degree, and 47% - hyperfunction of 1 degree, 56% have CD4 immune deficiency of 1 degree and 44% - 2 degree (Table 4.4).

In the humoral link, there was an immune deficiency of IgA and Ig G of 2 and 3 degrees, a transient increase in IgM degree I in 67.0% of children with RSLT.

Table 4.4

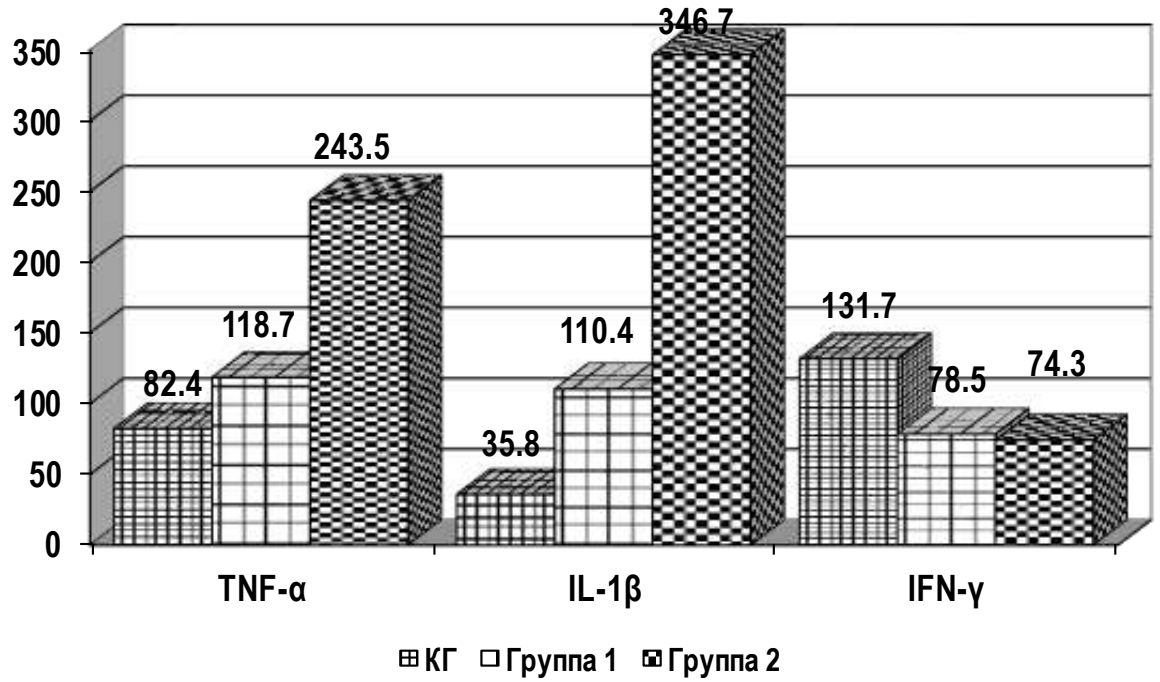
The degree of violations of the immune status of sick children with RSLT according to the results of frequency analysis

Indicators	The degree of immune disorders (SIR)					
	immune deficiency			Hyperfunction of the immune system		
	I degree (%)	II degree (%)	III degree (%)	I degree (%)	II degree (%)	III degree (%)
Leukocytes	26	0	0	46	28	0
Lymph.%	0	0	0	eleven	33	56
CD3, %	47	0	0	53	0	0
CD4, %	59	0	0	41	0	0
CD8, %	42	58	0	0	0	0
IRI	5	0	0	35	31	29
CD16, %	17	0	0	35	24	24
IgA	0	68	32	0	0	0
IgG	0	69	31	0	0	0
IgM	67	12	0	21	0	0

Formula of disorders of the immune system in patients: IgG_{2}^{-} $Ig\ A_{2}^{-}$ IgM_{1}^{+} $CD\ 4_{1}^{-}$ $CD\ 8_{2}^{-}$ $Lymph_{3}^{+}$ $CD3_{1}^{+}$ $Lake_{2}^{+}$ $CD16_{1}^{+}$.

4.3. Clinical diagnostic and prognostic significance of cytokines in primary and recurrent stenosing laryngotracheitis in children

According to the theory of polarization of the immune response, T-lymphocytes-helpers are responsible for the development of cellular immunity, and B-lymphocytes-helpers - humoral. .The main role in the regulation of the type of immune response and in the implementation of reciprocal relationships between them is played by cytokines:), γ-interferon (INF - γ), interleukins IL -1β, IL - 4 [288]. To establish the role of the cytokine spectrum in the development of primary and recurrent OSLT in children, we determined the level of interferons IFN-α and IFN-γ, the level of IL-4 and the level of pro-inflammatory cytokines : IL-1β, IL-6 (Fig. 4.1).



Rice. 4.1. The content of TNF -α, IL -1β and IFN -γ in the blood serum of children,
OSLT patients depending on the form of the disease

Our data show a significant dependence of the concentration of the level of pro-inflammatory cytokines in the blood serum on the form of OSLT. .Particularly

pronounced disorders were noted in children with RSLT. .The revealed changes significantly differed from the values obtained in the group of children with PSLT.

So, if during RSLT the level of serum TNF-α in the examined children was significantly higher (243.5±23.9 pg/ml compared with the data of children in the control group - 82.4±7.0 pg/ml, P <0.001) , then with PSLT only a moderate increase in this cytokine was noted (118.7±9.3 pg/ml, compared with the control P <0.05).

When analyzing the results of the study of the level of IL-1β in the blood serum, it was found that in children with RSLT there is an almost tenfold increase in its level compared to the control - 346.7±36.6 pg/ml, against 35.8±3.9 pg /ml (P <0.001).

In children with PSLT, there was an increase in the level of IL-1β by more than 3 times compared with the control group of children - 110.4±8.3 pg/ml (P <0.001).

As is known, IFN-γ is produced by activated Th 1-cells and NK - cells. .In our studies, a reduced level of IFN-γ compared to the control group of children was noted (Fig. 4.1). Moreover, this decrease is observed in OSLT: with RSLT - 74.3±4.9 pg/ml (P <0.001), with PSLT - 78.5±7.3 pg/ml (P <0.001) .this in the control group of children was on average 131.7±11.0 pg/ml.

Thus, when analyzing the level of a number of inflammatory cytokines in the blood serum of children with OSLT, compared with the control, we noted a significant significant increase in the level of TNFα and IL-1β with RSLT and a moderate increase in their serum levels with PSLT.

The serum level of IFN-γ during OSLT was significantly lower than in the control group and did not depend on its form..

As already mentioned, OSLT is characterized by predominant activation of type II T-lymphocytes . The main cytokine responsible for the immune response along the Th 2 pathway is interleukin-4, which, together with IL -12 and the CD 40 - CD 40 L molecular complex , are involved in starting the synthesis of antigen-

specific immunoglobulins class E (IgE) by B-lymphocytes [Tsarkova S. .A., Yastrebova E.B., Starikova M.G., 2001].

IgE -dependent activation of high-affinity receptors (FcεRI) of mast cells and basophils, as well as low-affinity IgE -receptors (FcεRII) of eosinophils leads to the release of a number of preformed and synthesized de novo biologically active substances with a wide range of pro-inflammatory properties that ensure the influx of activated effector cells from the peripheral blood into the bronchial system and the development of allergic inflammation [O . P. _ Zinkevich , V. _ M. _ Bondarenko , Vlu Delian et al ., 1999].

Interleukin-4 belongs to the cytokines capable of leading cells to the final differentiation and to the implementation of their effector functions. The main effects of IL-4 include the ability to switch the synthesis of IgG and IgM in B-lymphocytes to the synthesis of IgE [Timon S. I. , McAllister V. _ A. , Walsh M. , Cafferkey M. _ T. , 2009]. In addition to the induction of IgE synthesis, IL-4, acting on B-lymphocytes, increases their viability, size, expression of receptors for IgE and their own receptors for IL-4.

Along with clinical and anamnestic data, indicators of the function of external respiration and data from a laboratory study of the level of IgE in the blood and the concentration of IL-4 in various biological fluids are important as markers of inflammation activity.

The results of the study of the levels of IL-4 in the blood serum and in the smear, as well as the level of total Ig E in the blood serum of all examined children are presented in Table 4.5.

As can be seen from the table, increased levels of total IgE are detected in the peripheral blood of sick children. .The highest level is observed in the group of children with RSLT (362.0 ± 19.5 IU/l), which significantly exceeds the value of this indicator in children with PSLT (308, 0±13.5 IU/L) ($P < 0.05$) and with the control group (103.0±6.12 IU/L) ($P < 0.001$).

Thus, with RSLT, there is a higher content of IgE in the blood serum compared with children with PSLT. When studying the level of IL-4 in blood serum in children, a similar pattern was revealed: the highest level of IL-4 is typical for children with RSLT (15.1±0.63 pg/ml), which significantly (P <0.001) exceeds the value of this indicator in children with PSLT (12.0±0.38 pg/ml). In contrast to peripheral blood, in a smear taken from as close as possible to the focus of inflammation, the level of IL-4 is significantly (P <0.001) higher in children with PSLT (310.0±13.5 pg/ml) compared with the data of children suffering from RSLT (76.0±3.6 pg/ml).

Table 4.5

The content of IL-4 and Ig E in biological fluids of children with OSLT

Indicators	Control group (n=40)	1 group (n=122)	2 group (n=153)
IL-4 (smear), pg/ml	0	310.0±13.5***	76.0±3.6*** ^^^
IL-4 blood serum, pg/ml	2.85±0.19	12.0±0.38***	15.1±0.63*** ^^^
IgE in blood serum, IU/l	103.0±6.12	308.0±13.5***	362.0±19.5*** ^

Note: * - differences relative to the data of the control group are significant (* - P <0.05, ** - P <0.01, *** - P <0.001); ^ - differences between the data of groups 1 and 2 are significant (^ - P <0.05, ^^ - P <0.01, ^^^ - P <0.001)

The study of the level of cytokines in the oropharynx is devoted to a few works related to the pathology of the oral mucosa [64].

We have studied the cytokine profile of the oropharyngeal secretion in children with ASLT, taking into account the severity and stage of the disease (primary-recurrent). Investigated the content of three cytokines - IL-1 β , TNF- α and IL-4.

They were chosen as likely markers of total (IL-1 β , TNF- α) and allergen (IgE)-dependent phlogogenicity (IL-4).

In the group of healthy children, the content of IL-1 β in saliva was 21.8±1.80 pg/ml. According to the groups of patients, the following results were obtained:

group 2 - 196.0±20.76 pg/ml, group 1 - 128.0±14.04 pg/ml (for all indicators P<0.001). Differences between groups are significant (P<0.01) (Table 4.6).

In the control group, the content of TNF- α in saliva was 27.3±2.55 pg/ml. According to the groups of patients, the following results were obtained: group 2 - 95.7±9.16 pg/ml, group 1 - 54.6±4.56 pg/ml (for all indicators P<0.001).

Table 4.6

Cytokines in oral secretions in children with OSLT, depending on forms of the disease

Cytokine values, pg/ml	Control Group	1 group	2 group
IL-1β	21.8±1.80	128.0±14.04***	196.0±20.76*** ^^
TNF-α	27.3±2.55	54.6±4.56***	95.7±9.16*** ^^^
IL-4	6.2±0.41	12.7±1.02***	19.5±1.79*** ^^

Note: * - differences relative to the data of the control group are significant (* - P <0.05, ** - P <0.01, *** - P <0.001)

In healthy children, the content of IL-4 in saliva was 6.2 ± 0.41 pg / ml .. The following results were obtained in groups of patients: group 2 - 19.5 ± 1.79 pg / ml, group 1 - 12.7 ± 1 .02 pg/ml (for all parameters P<0.001).

As a result of the data obtained, it can be judged that the state of real homeostasis can be an indicator of pathological processes, including allergic inflammation [Zplatnikov A.L. , 2004].

In the present study, this manifested itself in the study of the cytokine profile (IL-1 β , TNF α and IL-4) of oropharyngeal secretion in children with OSLT. In the acute phase of the disease, the content of all three cytokines increased significantly. A significant and constant increase in performance was noted for IL-1 β. In patients with RSLT, the indices were higher than those with PSLT. This was observed for all three cytokines .. The difference is that with PSLT, there is usually no increase in serum levels of IL-1.β and TNFα .

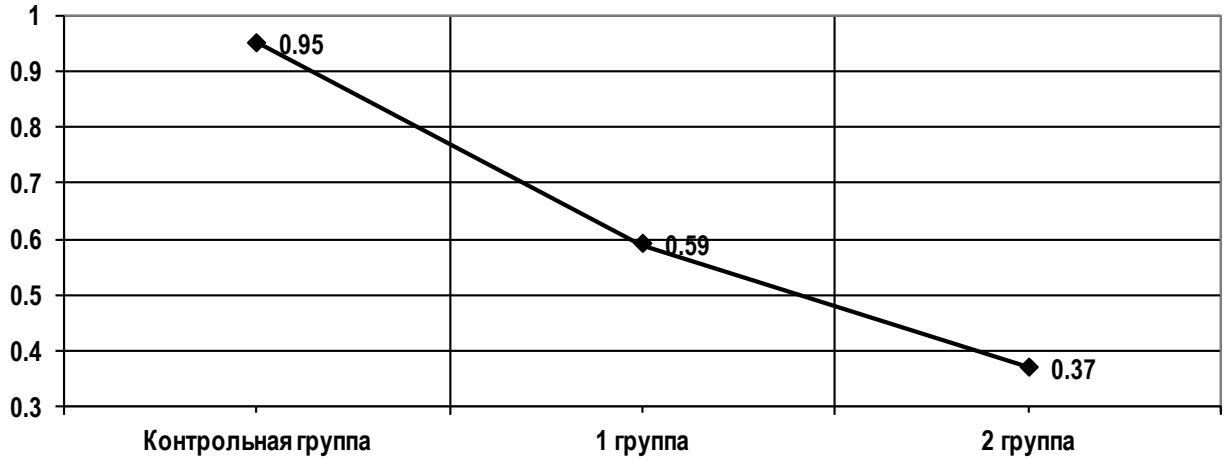
According to the literature, during an inflammatory reaction, to a greater extent due to the action of an infectious agent and to a lesser extent - in atopic inflammation, IFN-γ, activating the macrophage link of immunity, is a direct inducer of the synthesis of IL-1β [Masek V ., Sorli J. , Kopriva S. , Marin J , 2004; Wyatt J. , 2012]. Under physiological conditions, IL-1β is able to enhance the production of IFN-γ by activating Th1 cells.

Based on the foregoing, it seemed reasonable to us to conduct a correlation study between the concentrations of these cytokines depending on the form of OSLT .

As can be seen from Figure 4.2, the correlation analysis made it possible to establish the presence of a direct relationship between the content of IFN-γ and IL-1β in blood serum. .Thus, if in the control group the correlation coefficient was close to unity (r = 0.95), then in 1 and group 2, the values of the correlation coefficient were 0.59 and 0.37, respectively. Significant correlation coefficients between other pairs of cytokine levels were not obtained in any group.

Therefore, the results of our study confirm the existence of a relationship between the concentrations of IFN-γ and IL-1β, and this dependence is direct and decreases depending on the form of OSLT, which indicates violations of immunoregulatory mechanisms.

Therefore, a reduced serum INF-γ concentration indicates an impairment of IL-1β-mediated production of IFN-γ by Th-1 cells..



Rice. 4.2. Correlation coefficient values (r) between content in blood serum IFN-γ and IL-1β in various forms of OSLT

It is possible that activation of the macrophage link of immunity, which occurs during OSLT, may contribute to an increase in the production of substances by macrophages that inhibit the synthesis of IFN-γ.

Thus, it has been established that the majority of children with ASLT have a reduced content of T .- .cells T cells naturally affect the content of specialized phenotypes that perform helper and suppressor functions.

There is no doubt that a decrease or increase in their number can have a negative impact and, in all likelihood, is one of the pathogenetic factors of the inflammatory process. .As is known, NK cells play an important role in anti-infective protection, and their changes in both directions, due to several reasons: partial immunodeficiency, insufficient production of non-toxic antibodies that block the activity of immunocompetent cells [Bashkina OA, 2006].

One of the causes of immunodeficiency states is a violation in the body under the influence of various agents of immunoregulatory processes carried out with the help of Th1- and Th2-helpers .. 8, IL-12, INF, TNF, etc. .), the latter synthesize cytokines that stimulate humoral immunity (IL-4, IL-5, IL-10, transforming growth factor - IL-1 β, etc. .) .There is a certain balance in a normally functioning organism interactions between Th-1 and Th-2 helpers. But a significant change in their

activity under the influence of any influence can lead to serious adverse consequences in the functioning of the immune system as a whole..

It has been established that the allergic process causes the activation of Th2 helpers and the synthesis of cytokines that have a suppressive effect on cellular immunity. The .cytotoxic mechanism of damage is activated, which is associated with T-killers [Williams J. _ V. , Harris P. _ A. , Tollefson S. _ J. , 2014].

There was a direct relationship between a decrease in the level of T-suppressors/cytotoxic lymphocytes and an increase in B-lymphocytes and serum immunoglobulins of class G and A, reflecting the functional state of the B-immunity system..

Therefore, our results indicate a violation of metabolic processes and pronounced immunological changes that contribute to the development of complications of this disease..

4.4. Influence of endogenous intoxication on the state of immunological reactivity in OSLT children

More and more convincing evidence is accumulating that the increased incidence and severity of ASLT in children depend on the reactivity of the child, and a change in the specific and nonspecific reactivity of the homeostasis defense systems is the first and main condition for the development of the infectious process. In this regard, our next task was to study the effect of endogenous intoxication on the immunological reactivity of young children with OSLT.

Table 4.7 presents the results of studies of the immune system depending on the degree of intoxication in patients with OSLT in young children. When analyzing immunological parameters, it was found that in children during the height of the disease, a significant decrease in the content of leukocytes, the absolute number of lymphocytes, T-lymphocytes, T-helpers ($P<0.05-<0.001$) and a significant increase in T-suppressors (CD_8) and T-killers (CD_{16}), compared with the healthy group ($P<0.001$). An imbalance in the subpopulation composition of T-lymphocytes, namely a decrease in CD_4 and an increase in CD_8, indicates a sharp decrease in immunological reactivity and a direct dependence on the degree of endogenous intoxication.

One of the levels of anti-infective protection in OSLT is the phagocytic system. In healthy children, the phagocytic activity of neutrophils (PAN) was in the range of 55.2±1.6%. In the acute period of the disease, it was noted that the FAN index in OSLT was lower than in healthy children ($P<0.001$) for all degrees of endogenous intoxication. Another important peripheral population in children is B-lymphocytes. In healthy children, an average of 27.5±1.4% of B-lymphocytes circulate in the peripheral blood. With OSLT, the relative and absolute number of B-lymphocytes during the peak period significantly differs from their number in healthy children ($P<0.05-<0.001$) in the direction of decrease.

Dysimmunoglobulinemia was observed in children with ASLT in the acute period of the disease. Immunoglobulin IgG , Ig A and Ig M were significantly reduced, at all degrees of intoxication ($P<0.001$), in direct proportion to the severity of the clinical picture.

So, during the peak period, with I and II degrees of intoxication, the production of IgG was 1.4 times, and with III degree 2.2 times reduced, compared with healthy children. The concentration of serum Ig A in patients was significantly reduced compared with the data of the healthy group with I and II degrees of intoxication ($P<0.001$), and with III degree of intoxication it was 116.8±17.8 mg% versus 130±8.6 mg% ($P>0.05$). The concentration of Ig M in patients is significantly reduced compared to the data of the healthy group with II and III degrees of intoxication from 1.3 to 1.4 times ($P<0.001$), and with I degree of intoxication it was 108±7.2 mg% versus 115, 2 ± 8.2 mg% ($P>0.05$). These indicators indicate a reduced antimicrobial immunity and a decrease in the antitoxic properties of the body. Thus, the observed sample can be characterized as a sample with significant metabolic and immune status disorders, the pronounced fluctuation ranges of the studied parameters (Table 4.7) made it possible to count on the achievement of the goal in further analysis.

We carried out a correlation analysis of immunological parameters in sick children, depending on the severity of the process, during the period of clinical recovery.

The conducted studies showed an inversely proportional dependence of the vast majority of immunological parameters (T-lymphocytes $r = -0.88$ ($P<0.01$), and their subpopulations; T-helpers - $r = -0.24$; ($P<0.05$), IgG $r =-0.66$ ($P<0.01$) on the severity of the degree of endogenous intoxication in patients with OSLT in young children.

Thus, the immunological studies carried out at the height of OSLT in children indicate the development of immunological deficiency of both the cellular and

humoral levels. An inversely proportional dependence of indicators on the degree of endogenous intoxication was revealed.

Summarizing the presented data, it should be noted that OSLT is a very urgent problem already because of its wide prevalence .. In turn, the inflammatory process in the larynx leads to a decrease in immunological parameters, and the present allergic background activates T-lymphocytes, which explains the imbalance of immunological parameters. And all this indicates the participation of not only the inflammatory process, but also the allergization of the body of sick children.

And the noted systemic and local immunological changes can be qualified as a secondary immunodeficiency state.

CHAPTER V. _ COMPARISON OF THE CLINICAL COURSE OF SLT WITH THE CHARACTER OF UPPER MICROFLORA DISTURBANCES RESPIRATORY IN CHILDREN

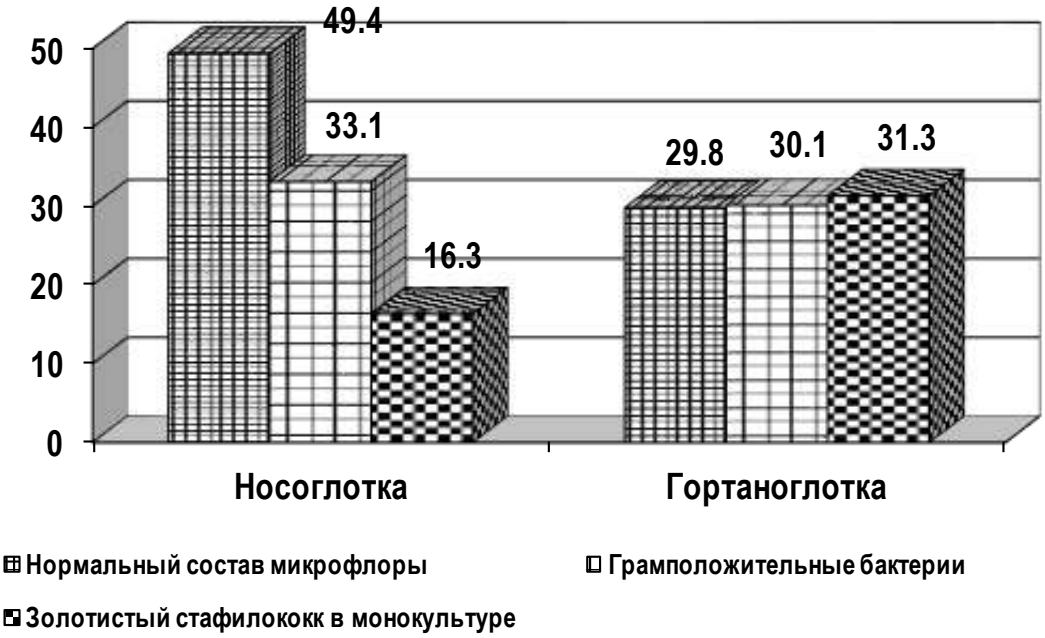
In 275 children aged 6 months to 7 years with recurrent stenosing laryngotracheitis, the microbial landscape of the mucous membranes of the upper respiratory tract (URT) was studied using conventional methods of bacteriological research, including sowing the discharge of the nasopharynx and laryngopharynx on nutrient media with subsequent identification. The microflora of the respiratory tract in our studies was assessed during primary and recurrent SLT in the acute period (from the 1st to the 5th day of the illness) and during the remission period (from the 6th day of the illness).

The microbial landscape was assessed at the first stenosis of the larynx and at its recurrence against the background of acute respiratory viral infections in the acute period (from the 1st to the 7th day of illness) before the start of antibiotic therapy and in the period of full health (at least 10-14 days after the respiratory viral and /or bacterial infection). Not only the qualitative microbiological landscape was taken into account, but also its quantitative content.

In the acute period of viral infection, only 87 (31.6%) children in the nasopharynx and 52 (18.1%) children in the laryngopharynx had a normal microflora composition.

Dysbiotic processes were characterized by the colonization of the mucous membranes of the upper respiratory tract by pathogenic and conditionally pathogenic gram-positive and gram-negative flora, a decrease in the release of saprophytic and normal microflora. Undoubted leadership in this process has Staphylococcus aureus. It occurs both in the form of a monoculture and in the form of associations - in combination with other pathogenic pathogens. Along with gram-positive bacteria, fungi of the genus Candida were detected , as well as Klebsiella, E. coli, Enterobacter, Moraxella , which formed complex associations.

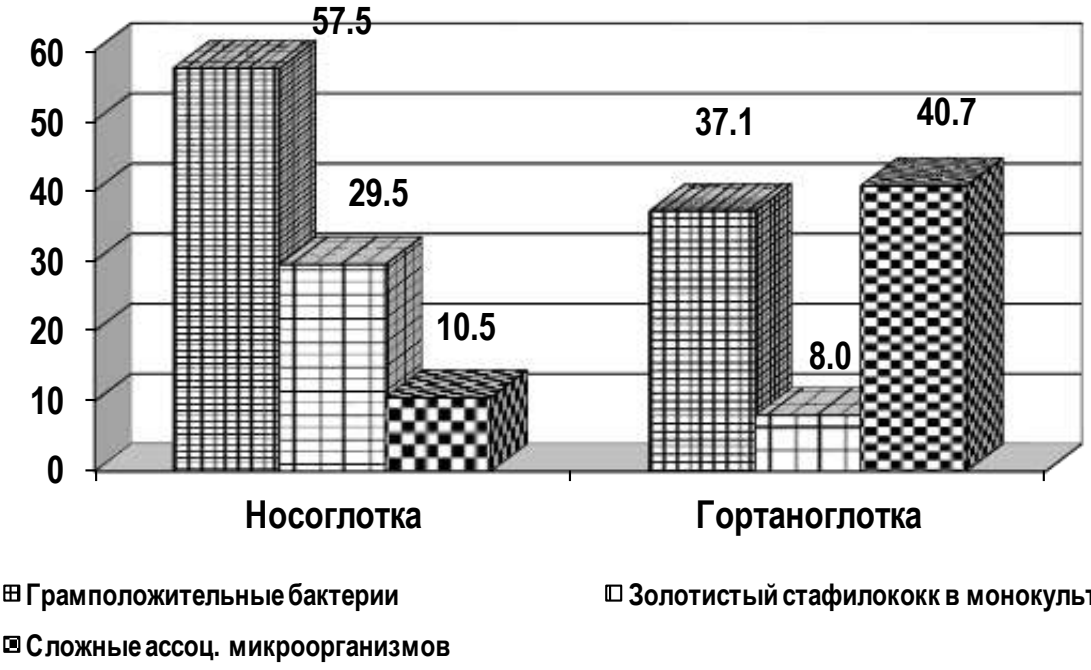
We analyzed the composition of the microbiocenosis of the respiratory tract depending on the number of episodes of laryngeal stenosis on the background of a viral infection. In patients with 3 episodes of stenosing laryngotracheitis (SLT), the normal composition of the microflora of the nasopharynx was recorded in 136 (49.4%) of the examined children, in the laryngopharynx - in 82 (29.8%). In other cases, gram-positive bacteria were most often detected in 91 (33.1%) in the nasopharynx and in 85 (30.1%) in the laryngopharynx and Staphylococcus aureus in monoculture (45 (16.3%) and 86 (31.3%)), that is, microbial communities were formed that characterize the I degree of dysbiosis. Associations of gram-positive with gram-negative microbes (II degree of dysbiosis) were rare - in 18 (6.5%) cases in the nasopharynx and in 27 (9.8%) - in the laryngopharynx.



Rice. 5.1. The composition of the microbiocenosis of the respiratory tract, depending on the number of transferred episodes (3 episodes) of stenosis of the larynx

In children with 4-5 cases of stenosis of the larynx in the acute period of viral infection, normal microflora in the upper respiratory tract was determined in a third of patients. The pathogenic flora of the nasopharynx in the acute period is mainly represented by associations of gram-positive bacteria 158 (57.5%), a monoculture of Staphylococcus aureus is quite often found - in 81 (29.5%) cases. Complex as-

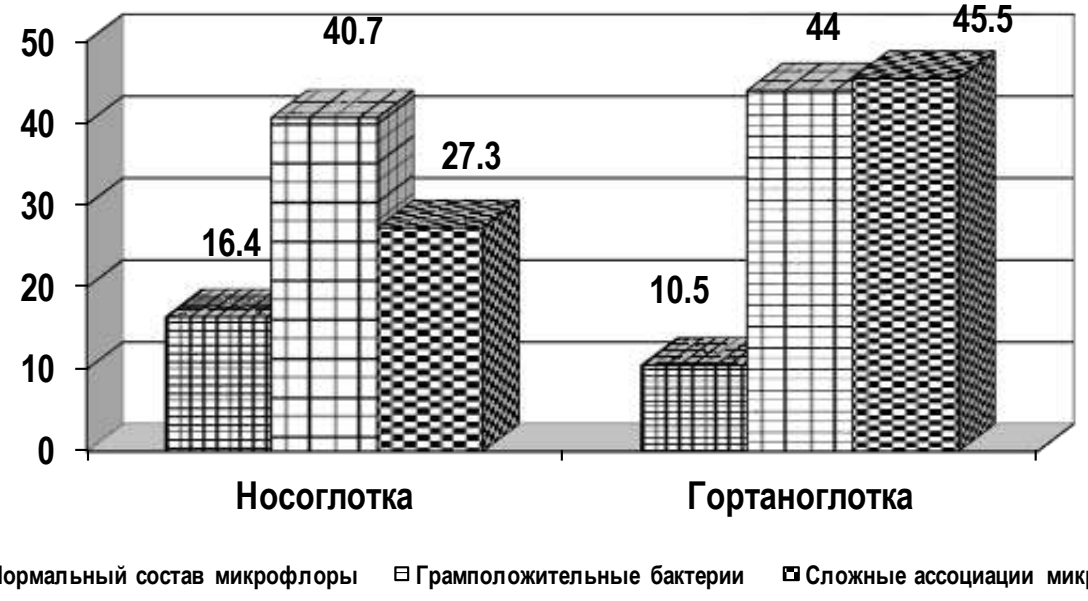
sociations of microorganisms were registered in 29 (10.5%) children. In the laryngopharynx in the same patients, the composition of the microbiocenosis changes somewhat - the proportion of gram-positive flora 102 (37.1%) and the monoculture of staphylococcus 22 (8.0%) decreases, the number of patients with complex associations of microbes increases significantly - up to 112 (40.7 %), gram-negative microorganisms that are unusual for this econiche appear in monoculture - in 29 (10.5%) of the examined. In the period of convalescence of acute respiratory viral infections, microbiocenosis is represented in the nasopharynx mainly by Staphylococcus aureus in monoculture in 162 (58.9%), there are almost no complex associations -15 (5.5%). In the laryngopharynx, complex associations were more often recorded; 98 (35.6%) percentage of children with S. aureus on the mucous membranes in monoculture remains high.



Rice. 5.2. The composition of the microbiocenosis of the respiratory tract, depending on the number of transferred episodes (4-5 episodes) of stenosis of the larynx

In children with 6 or more episodes of SLT against the background of ARVI, the normal composition of the microflora in the period of acute infection was determined in the nasopharynx in 45 (16.4%) of the examined patients and in 29

(10.5%) - in the laryngopharynx, in the period of convalescence in 55 (20.0%) and 42 (15.3%) respectively. Dysbiotic disorders in the nasopharynx in the acute period were expressed by an increase in the proportion of children with complex associations of microbes 75 (27.3%), and the preservation of the leading role of gram-positive flora 112 (40.7%). In the laryngopharynx, there is a significant (12.5%) growth of allochthonous flora - E. coli, Enterobacter, Moraxella , fungi of the genus Candida and their associations with gram-positive microbes 121 (44.0%) with a decreasing role of gram-positive pathogens 72 (26.2%). In the period of convalescence in the nasopharynx of these children, gram-negative microorganisms also began to be detected in a monoculture 17 (6.2%), the percentage of gram-positive microbes 34 (12.4%) decreases, there is a significant increase in Staphylococcus aureus and complex associations of bacteria by 42%. In the laryngopharynx, the microflora is represented by complex associations - in 125 (45.5%) children, a decrease in the role of gram-positive microbes and an increase in the percentage of allochthonous flora to 6.7%.



Rice. 5.3. The composition of the microbiocenosis of the respiratory tract, depending on the number of transferred episodes (6 or more episodes) of stenosis of the larynx

The indicators of the proportion of different microorganisms in the overall structure of the isolated microflora do not quite adequately reflect their etiological role in the development and maintenance of the infectious process. More evident is the indicator of infectivity - the percentage of patients in whose material at any stage of the examination (in any of the periods of exacerbations) at least 1 time a particular pathogen was detected. So, in patients with RSLT, *S. aureus*, β-hemolytic streptococcus, fungi of the genus *Candida* were isolated in 49.5%, 28% and 22.5%, respectively. A characteristic of the etiological significance of clinical isolates is also the indicator of constancy - the proportion of samples containing a certain type of microorganisms. In α-hemolytic streptococcus and *S. aureus* , the constancy rate was 33.6% and 53.9%, in fungi of the genus *Candida* 28.6%, which confirms their participation in the formation and maintenance of dysbiosis of the mucous membranes of the upper respiratory tract. When comparing the clinical course of SLT with the nature of dysbiotic disorders, it was revealed that the disease is characterized by more pronounced fever and intoxication in children who do not have microflora disorders. With dysbiosis of I and II degrees, the disease occurs against the background of unexpressed or absent toxicosis at subfebrile or normal temperature. In children with grade II dysbiosis on the mucous membranes of the upper respiratory tract, we noted the frequent development of laryngeal stenosis of the second degree, a significant increase in the duration of cough, the severity of catarrhal syndrome, and a "rich" auscultatory picture in the lungs compared with children with a normal composition of the microflora of the upper respiratory tract. The frequency of recurrence of SLT was also in direct correlation with the nature of the identified dysbiotic disorders.

Thus, it was determined that in children suffering from RSLT, there are significant violations of the microbiocenosis of the mucous membranes of the upper respiratory tract. Our study showed the phasing of the ongoing violations. In children who underwent the first stenosis of the larynx against the background of ARVI, in the acute period and in convalescence, the microflora of the upper respirato-

ry tract is represented mainly by gram-positive microorganisms. As the number of episodes of stenosis of the larynx increases, the "usual" gram-positive flora is displaced first by a monoculture of S. aureus, then it is gradually replaced by gram-negative microorganisms and allochthonous flora.

Dysbiotic disorders, maintaining a chronic inflammatory process on the mucous membranes of the upper respiratory tract, provide a worsening of the degree of stenosis of the larynx, an increase in the duration of cough, changes in the lungs and are a risk factor for recurrence of stenosing laryngotracheitis.

The same trend towards a decrease in the number of children with a normal - microbial landscape in the nasopharynx can be traced during RSLT and during remission. With PSLT during this period, the normal composition of the microflora of the nasopharynx is present in 60% of the examined, and only in 18% - with RSLT. During the period of remission with RSLT, we noted a 2.3-fold decrease in the number of children with normal laryngopharyngeal microflora compared with children who underwent PSLT. The conducted studies showed that during RSLT, the microflora of the nasopharynx is more susceptible to dysbiotic processes, and during the period of remission, the laryngopharynx is more susceptible.

The composition of the normal microflora of the upper respiratory tract in the acute period, both with primary and recurrent SLT, is mainly represented by a-hemolytic streptococcus (up to 91% in the laryngopharynx with PSLT, up to 75% with RSLT) and epidermal staphylococcus aureus (47% in the nasopharynx with PSLT). , 56% for RSLT). Micrococcus in the nasopharynx in the acute period is detected with PSLT almost 5 times more often than with RSLT (19% and 4%, respectively). In PSLT, the proportion of pigmented neisseria in the laryngopharynx is high, both in the acute period and in remission (64 and 100%, respectively). Saprophytic Neisseria in the acute period are more often part of the normal microflora in RSLT (46%), and saprophytic corynebacteria predominate in PSLT (24%). During the period of remission, the predominant growth in the laryngopharynx of α-hemolytic streptococcus also remains, both with PSLT (91%) and RSLT (75%).

With PSLT during remission, the proportion of pigmented (up to 100% in the nasopharynx) and saprophytic (75% in the laryngopharynx) Neiss series increases, while Micrococcus, Staphylococcus epidermidis, and saprophytic corynebacteria are either absent or detected in single patients. In the nasopharynx during the acute period with PSLT, micrococcus is recorded in 19% of cases, during the remission period even more often - up to 22%. Saprophytic corynebacteria in the acute period are isolated from the nasopharynx during PSLT in 24% of cases. The proportion of epidermal staphylococcus in RSLT during remission decreases to 44%, and a-hemolytic streptococcus is detected in the nasopharynx only in 11% of the - examined. Pigmented neisseria during remission in the nasopharynx in children who underwent PSLT were not registered .

We compared the nature of dysbiotic changes in the respiratory tract in the acute period of the disease depending on the age of our patients and noted the frequent damage to the mucous membranes by Staphylococcus aureus in all age periods. In the acute period of PSLT in children older than 3 years the most pronounced violations of the microbiocenosis of the mucous respiratory tract are determined, both in the nasopharynx and laryngopharynx (the normal composition of the microflora is present in 9.5% and 9% of the examined, respectively). With RSLT in the acute period, we did not reveal such a pattern . In the period of remission with PSLT, the normal microbiological composition of the respiratory tract is restored only in half of those examined from 0 to 3 years old, at an older age, the normal composition of the flora in the nasopharynx in 33% of children aged 3-6 years and in 22% of children aged 6 years and older. The normal microbial landscape of the laryngopharynx in children under 3 years of age during remission with PSLT was determined in 50% of cases, in the other two groups - only in 25%. With RSLT during remission, the restoration of normal flora from 0 to 3 years was noted only in 16%, over 3 years - in 50% of cases, the microflora remains normal.

In the acute period, significant changes in the microbiocenosis of the respiratory tract were noted both in primary and recurrent SLT. Dysbiotic processes were

characterized by the colonization of the mucous membranes of the upper respiratory tract by pathogenic and conditionally pathogenic gram-positive and gram-negative flora, a decrease in the release of saprophytic and normal microflora. Undoubted leadership in this process in the acute period of the disease has Staphylococcus aureus. It occurs both in the form of a monoculture and in the form of associations - in combination with other pathogenic pathogens. Infection by Staphylococcus aureus of the respiratory tract in the acute period is high in both PSLT and RSLT. During PSLT in the acute period, Staphylococcus aureus was isolated from the nasopharynx in 28% of the examined children, and in 25% from the laryngopharynx. With RSLT, this microbe was found in 39% of cases in the nasopharynx and in 23% of children in the laryngopharynx. in associations *S. _ aureus* more often inoculated in patients with RSLT from the laryngopharynx - in 22% of cases.

In the acute period of the disease, α-hemolytic streptococcus is determined more often in the laryngopharynx in patients with PSLT (17%), with RSLT, it was determined very rarely (in 2% of cases). Both in PSLT and RSLT in the acute period, *E. coli is found on the mucous membranes of the upper respiratory tract* (6 and 8% respectively). Mushrooms of the genus *Candida* in the laryngopharynx with PSLT were detected in 25% of cases, with RSLT - in 18%, mycelium of the fungus was also isolated from the nasopharynx, both with PSLT and RSLT. Complex associations of microorganisms were not observed only in the pharynx in patients with PSLT; with RSLT, they were found both in the nasopharynx (15%) and in the laryngopharynx (23% of the examined). Gram-positive pathogens in the acute period of SLT occur mainly in the form of associations, mainly with Staphylococcus aureus, and do not have such a high representation in the URT as *S. _ aureus* .

In RSLT in the acute period of the disease, complex associations of pathogens were more common in older children in the laryngopharynx (43%) (Fig. 6). The presence of such changes in microbiocenosis characterizes the severity of dysbiotic processes and the duration of their existence. With PSLT in the acute period, the

above patterns are not detected, although pathogens such *as* Candida , E. coli , Klebsiella are more often isolated from older children. Infection of the mucous membranes of the respiratory tract by Staphylococcus aureus in the period of remission very high, both in primary and recurrent SLT. But with RSLT, the process of colonization of mucous membranes by this pathogen is more pronounced. With PSLT, the level of excretion S. _ aureus from the nasopharynx at the level of 32%, with RSLT it reaches almost 50%. (3-hemolytic streptococcus occurs in RSLT only in the form of associations, and only in the laryngopharynx - up to 17% of cases, with PSLT, β-hemolytic streptococcus occurs in the nasopharynx as a monoculture - up to 7%, in the laryngopharynx in the form of associations - up to 20% of the examined Pneumococcus with PSLT is detected in the respiratory tract during remission in 13%), with RSLT - only in the laryngopharynx in 12% of the examined. Complex associations of pathogens during remission occur with RSLT in the nasopharynx almost 2 times more often than with PSLT. In the laryngopharynx, complex combinations of pathogens with PSLT during remission are detected quite often - in 33%, with RSLT - in 26%. Both in the acute period and during remission, phenomena of deepening of dysbiotic processes in the nasopharynx are found during RSLT.

Mushrooms of the genus Candida with PSLT from the nasopharynx during remission, they are not detected, with RSLT they are determined in 3% of the examined. In the laryngopharynx, the frequency of detection of these pathogens in primary and recurrent SLT is approximately the same - 20%. Klebsiella was not detected in the respiratory tract during remission with PSLT , with RSLT it is detected in 3% of cases. Identification *of E. coli* from the nasopharynx during primary and recurrent SLT is approximately at the same level and amounts to 7 and 6%, respectively. Colonization of the laryngopharynx by this pathogen with RSLT increases almost 2 times compared with PSLT - 12 and 7%, respectively. The normal flora is represented in the period of remission, as well as in the acute period, both in primary and in recurrent SLT, mainly by α-hemolytic streptococcus.

During the period of remission, the isolation of Staphylococcus aureus from the mucous membranes of the respiratory tract during PSLT was observed more often in children aged 3 to 6 years. As a monoculture *S. _ aureus* isolated in 100% of these children from the nasopharyngeal mucosa, and in 50% from the laryngopharynx. In children of this age, a high frequency of isolation of fungi of the genus Candida (75%), pneumococci (50%), complex associations of microorganisms (75%) and the most aggressive pathogens - S. _ haemolyticus (25%) *and* E. coli (25%). In children of early age, the composition of the microflora of the upper respiratory tract in the period of remission is mainly represented by Staphylococcus aureus and pneumococcus (14% each). At an older age, the leadership remains with Staphylococcus aureus (50%), pneumococcus (25%) and complex microbial associations (50%).

With RSLT, the isolation of Staphylococcus aureus from the mucous membranes of the upper respiratory tract was noted in children of all age groups, reaching 83% in older children (in the nasopharynx and laryngopharynx). Complex combinations of pathogens and microorganisms such *as* E. coli , S. haemoyiticus and mushrooms of the genus Candida are determined during the period of remission mainly in children of the older age group. In children aged 3-6 years, the main representatives of the microflora were S. _ aureus , pneumococcus, hemolytic staphylococcus (42, 17 and 17% respectively). In this age group, we noted the absence of isolation of gram-negative bacteria - Klebsiella, E. coli , as well as α-hemolytic streptococcus. Despite the frequent prescription of antibacterial drugs in children of this age, fungi of the genus Candida and complex associations from the laryngopharynx were determined only in 8%) of the examined.

With recurrence of SLT at an early age and during remission, a high degree of contamination of the mucous membranes of the upper respiratory tract with Staphylococcus aureus (in 20%), α-hemolytic streptococcus (20%), and complex associations (30%) is noted. A significant reduction in excretion has been established S. _ aureus from mucous membranes of the upper respiratory tract compared with the

acute period (from 83 to 20%), and the proportion of α-hemolytic streptococcus at this age (remission period) increases from 0 to 20%, an increase in seeding was also noted E. coli (from 0 to 10%) and complex associations (from 0 to 30%).

Table 5.1

Cytological parameters of the mucous membrane of the respiratory tract in patients with primary and recurrent SLT in the acute period (number of cells in %)

Indicators	acute period			
	PSLT		RSLT	
	noso pharynx	laryngopharynx	noso pharynx	laryngopharynx
Neutrophils	88.9 ±4.4	83.1 ±4.2	81.4 ±4.1	87.1 ±4.4
Lymphocytes	7.5 ±0.30	14.6 ±0.58	11.6 ±0.46***	15.6 ±0.62
Eosinophils	0.45 ±0.02	1.13 ±0.06	1.76 ±0.09***	0.66 ±0.03***
Macrophages	0	0	1.38 ±0.04	0

Note: * - differences relative to PSLT data are significant (*** - P <0.005)

Table 5.2

Cytological parameters of the mucous membrane of the respiratory tract in patients with primary and recurrent SLT in the period of incomplete remission (number of cells in %)

Indicators	period of incomplete remission			
	PSLT		RSLT	
	noso pharynx	laryngopharynx	noso pharynx	laryngopharynx
Neutrophils	89.8 ±4.5	77.3 ±3.9	86.9 ±4.3	84.7 ±4.2
Lymphocytes	9.01 ±0.36	22.75 ±0.91	9.9 ±0.40	15.29 ±0.61***
Eosinophils	0	0	1.14 ±0.06	0
Macrophages	0.25 ±0.01	0	0	0

Note: * - differences relative to PSLT data are significant (*** - P <0.005)

Thus, the identification of complex associations of microorganisms, long-term persistence of pathogens in RSLT demonstrates a certain degree of dysbiotic disorders of the respiratory tract in this disease.

During SLT, we noted an aggravation of the process of respiratory tract dysbiocenosis , characterized by the colonization of the respiratory tract mucosa, first by pathogenic gram-positive flora, then by the addition of gram-negative microflora, and even microorganisms that are unusual for this econiche. According to this feature - the nature of associations of microorganisms of the respiratory tract and the severity of dysbiotic processes - patients with primary and recurrent SLT were divided into three degrees to assess the severity of existing dysbiotic disorders. First degree - patients with normal microflora on the mucous membranes of the nasopharynx and laryngopharynx. The second degree - children who excrete pathogenic gram-positive pathogens in the form of a monoculture or in associations. For the most part this *S. _ aureus* , α -hemolytic streptococcus, as well as hemolytic staphylococcus, pneumococcus and others. Third degree - children with SLT, in which complex associations of microorganisms are determined (in addition to the above , there are also representatives of gram-negative flora, as well as fungi of the genus candida *)*. We also included in this degree the children isolating a monoculture of gram-negative pathogens or microorganisms that are unusual for this econiche, for example , E. coli .

In the groups of children identified by us with varying degrees of severity of dysbiotic disorders of the upper respiratory tract, we analyzed the clinical course (main manifestations) in primary and recurrent SLT .

Identification of 6 indicators for assessing the clinical course (the severity of intoxication, the presence of fever, the severity of catarrhal phenomena , the severity of dyspnea, the nature of the cough, physical data), and for RSLT, the recurrence rate for 12 months was also evaluated.

The severity of symptoms was assessed in points. The degree of intoxication: 0 points - no intoxication, 1 point - mild and short-lived symptoms during 1-2 days of illness, 3 points - severe symptoms of intoxication that persist after the 5th day of illness. Fever: 0 points - its absence, 1 point - subfebrile temperature, 2 points - febrile from 38 to 39 ° C, 3 points - above 39 ° C. Catarrhal syndrome: 0 points -

its absence, 1 point - meager symptoms in the form of moderate hyperemia of the mucous membranes of the laryngopharynx, 2 points - moderately expressed in the form of nasopharyngitis, 3 points - very pronounced and long-term (more than 5 days) persisting. Severity of dyspnea: 0 points - its absence, 1 point - slight dyspnea, detected only with anxiety and exertion, 2 points - dyspnea exists at rest, but without involvement of the auxiliary respiratory muscles in the act of breathing, 3 points - severe dyspnea with involvement of the act of breathing additional muscles. The nature of the cough: 0 points - its absence, 1 point - mild and persisting for no more than three days, 2 points - rough, dry, hacking, up to 5 days of illness, 3 points - persistent, rough unproductive more than 5 days of illness . Physical data: 0 points - the absence of any physical symptoms, 1 point - the presence of hard breathing, 2 points - the presence of dry rales scattered throughout the lung fields, 3 points - an abundance of rales of various calibers, as well as dry whistling rales.

The data obtained indicate that the level of severity of intoxication symptoms during PSLT is quite high in all groups and does not have significant differences depending on the degree of violation of the microbiocenosis of the respiratory tract of the upper respiratory tract and averaged 1.8 points (Table 5.3) .

Table 5.3

The severity of clinical manifestations (in points) of the main symptoms of P SLT depending on the dysbiotic manifestations of the upper respiratory tract

The degree of clinical manifestations of the acute period of PSLT	The degree of dysbiotic disorders of the upper respiratory tract		
	I degree	II degree	III degree
Expression and toxicity	1.88 ±0.09	1.77 ±0.09	1.82 ±0.09
Fever	1.63 ±0.07	1.32 ±0.05***	0.94 ±0.04*** ^^^
Catarrhal phenomena	1.63 ±0.08	2.17 ±0.11***	2.06 ±0.10**
The nature of shortness of breath	1.13 ±0.05	1.10 ±0.04	1.06 ±0.04
The nature of the cough	1.50 ±0.05	1.41 ±0.04	1.53 ±0.05
Physical data	1.88 ±0.08	1.20 ±0.05***	1.30 ±0.05***
Recurrence rate	1.88 ±0.09	1.77 ±0.09	1.82 ±0.09

Note: * - differences relative to grade I data are significant (** - P <0.01, *** - P <0.001); - differences relative to grade II data are significant (^^^ - P <0.001)

With RSLT in children assigned to groups I and II, the degree of severity of intoxication syndrome is approximately at the same level - 1.5 points, and in those examined from group III it is significantly higher (1.85 ± 0.54), i.e. on average 0.3-0.8 points higher than in children with less severe disorders of the microflora of the upper respiratory tract. In general, with PSLT, the disease occurs in all three groups with more pronounced symptoms of intoxication than with RSLT, especially in children from groups I and II; in children of group III, the indicator has a value similar to PSLT (Table 5.4).

Table 5.4

The severity of clinical manifestations (in points) of the main symptoms of RSLT in the acute period, depending on dysbiotic manifestations of the upper respiratory tract

The degree of clinical manifestations of the acute period of RSLT	The degree of dysbiotic disorders of the upper respiratory tract		
	I degree	II degree	III degree
Expression and toxicity	1.50 ±0.08	1.53 ±0.08	1.85 ±0.09** ^^
Fever	1.30 ±0.05	1.06 ±0.04***	1.08 ±0.04***
Catarrhal phenomena	1.56 ±0.08	1.56 ±0.08	1.76 ±0.09
The nature of shortness of breath	1.00 ±0.04	1.08 ±0.04	1.00 ±0.04
The nature of the cough	1.30 ±0.04	1.44 ±0.04*	1.58 ±0.05*** ^
Physical data	1.36 ±0.05	1.28 ±0.05	1.20 ±0.05*
Recurrence rate	1.45 ±0.07	1.80 ±0.09**	2.09 ±0.10*** ^

Note: * - differences relative to grade I data are significant (* - P <0.05, ** - P <0.01, *** - P <0.001); ^ - differences relative to the II degree data are significant (^ - P <0.05, ^^ - P <0.01)

The index of fever severity is higher in children from group I and is 1.63±0.64, it decreases by an average of 0.3 points in children of group II and significantly differs downward to 0.94±0.66 in children of group III groups. With RSLT, the severity of fever is the highest in group I and has no significant differences, being approximately at the same level in children of groups II and III (comprising 1.08±0.8 and 1.08±0.79 points, respectively). On average, the severity of fever symptoms in children with RSLT is lower than with PSLT, which is consistent with the literature [Sergeeva S. A., Kladova O. V., Uchaikin V. F., 2002; Khasanov S.A., Vakhidov N.Kh., 2007].

Catarrhal syndrome is more pronounced with PSLT in children of groups II and III and averaged 2 points. In children of group I, the value of this indicator is -

1.63±0.62. With RSLT, the indicator of the severity of catarrhal phenomena is significantly less than with PSLT, and amounts to 1.56±0.66, respectively, in children of group I, 1.55±0.62, group III - 1.76±0.86 points , which has a practically comparable value and is 0.5 points less than in general with PSLT. According to our data, in almost 1/3 of children with RSLT, the disease proceeds without pronounced catarrhal phenomena and against the background of normal temperature.

As for the severity of shortness of breath and the nature of cough, in all groups of subjects, both in primary and recurrent SLT, these symptoms do not have significant differences and are approximately the same. Thus, the severity of shortness of breath with PSLT averaged 1.1 points, with RSLT - 1 point, the nature of the cough - 1.5 and 1.4 points, respectively. Physical changes in the lungs were more pronounced with PSLT in group I and amounted to 1.88±0.66 points. In children belonging to this group, rich physical symptoms are more common, including multiple, different-sized, rather long-lasting wheezing. In children of grades II and III, the severity of this symptom with PSLT is at the level, respectively . In children with RSLT, rich physical symptoms were also noted in the examined, assigned to group I, the degree of its severity was estimated at 1.36±0.5 points, in groups II and III, respectively, 1.28±0.7 and 1.2± 0.55.

With RSLT, the recurrence rate of SLT steadily and significantly increases in groups of children with various severity of dysbiotic disorders in the upper respiratory tract. In children of group I it is 1.45±0.66 points, in group II 1.9±0.56 and in group III 2.09±0.58 points.

Thus, when comparing the clinical course of SLT with the nature of the - violation of the microflora of the upper respiratory tract, it was revealed that the disease proceeds with a more pronounced picture of intoxication and with a more pronounced fever in children who do not have deviations in the characteristics of the microflora in the upper respiratory tract. With the aggravation of dysbiotic manifestations, the disease proceeds against the background of unexpressed or absent toxicosis and often at normal temperature. The survey showed that with the

aggravation of the processes of dysbiosis, the risk of relapse of SLT increases significantly .

lysozyme activity in children with primary and recurrent SLT in the acute period and in remission was also considered as a marker of the severity of respiratory tract dysbiocenosis. In the acute period with PSLT, the activity of salivary lysozyme corresponded to the standard values (from 17 to 25%). During the period of remission, activity indicators decrease slightly, but in most cases they constitute the lower limit of the norm.

Table 5.5

The level of salivary lysozyme (in%) in patients with primary and recurrent O SLT, depending on the age of the patient and the period of the disease

Periods of diseases	Age	OSLT Forms	
		PSLT	RSLT
Acute period	From 3 months up to 1 year	17.2 ±0.86	26.1 ±1.31***
	2-3 years	22.3 ±0.89	25.5 ±1.02*
	Over 3 years old	31.8 ±1.59	28.8 ±1.44
Remission period	From 3 months up to 1 year	14.6 ±0.58	13.3 ±0.53
	2-3 years	20.8 ±0.62	21.7 ±0.65
	Over 3 years old	18.2 ±0.73	17.3 ±0.69

Note: * - differences relative to PSLT data are significant (* - P <0.05, *** - P <0.001)

With RSLT in the acute period of the disease, very high figures of lysozyme activity are detected, exceeding the norm by 1.5-2 times, and during the remission period with RSLT, the lowest indicators are recorded, which also differ from normal by 1.5-2 times.

Table 5.6
Salivary lysozyme activity (in %) depending on the severity of dysbiotic - manifestations of the upper respiratory tract in OSLT

OSLT Forms	The severity of dysbiotic manifestations of the upper respiratory tract		
	I degree	II degree	III degree
PSLT	4.75 ±0.24	24.44 ±1.22***	16.09 ±0.80*** ^^^
RSLT	21.4 ±0.86	29.6 ±1.18***	15.3 ±0.61*** ^^^

Note: * - differences relative to grade I data are significant (*** - P <0.001); ^ - differences relative to grade II data are significant (^^^ - P <0.001)

When analyzing the activity of lysozyme depending on age (Table 5.5), it was found that with PSLT in the acute period of the disease, as well as in the period of remission, in children from 3 to 6 and from 6 to 15 years, the activity of lysozyme corresponds to the norm. In children aged 0 to 3 years, the activity of lysozyme in the acute period is the lower limit of the norm, it decreases during the remission period, in most cases making up 1/2 of the normative indicator. With RSLT in the acute period of the disease, in all age periods, salivary lysozyme exceeds the normative indicator by 5-10%, and during the period of remission, the lowest activity of lysozyme was also noted in children from 0 to 3 years old, at 3-6 years old it corresponds to the norm and decreases in children older than his age by 5-10% of the norm.

The level of salivary lysozyme activity during SLT depends on the period of the disease. Lysozyme, as a marker of the state of nonspecific reactivity of the organism, during the period of remission can indirectly characterize the state of microbiocenosis of the mucous membranes of the upper respiratory tract, since in the presence of pathogenic and opportunistic microflora with antilysozyme activity in the respiratory tract, the level of lysozyme during this period can be very low. High, 2-3 times higher than normal, the level of lysozyme during remission indi-

cates that there are foci of chronic inflammation in the body , especially ENT organs that require sanitation and are in a state of active inflammation at the time of examination.

In the acute period of the disease, an increase in lysozyme activity also - indicates a microbiological problem, since with a high degree of dysbiosis, lysozyme is compensatory increased due to the production of the macrophage system and other blood cells involved in the inflammatory process. A decrease in lysozyme in the acute period of the disease is prognostically unfavorable, as it indicates a low immunological reactivity of the body, including nonspecific protective factors.

We analyzed changes in the activity of salivary lysozyme in children with PSLT, the activity of salivary lysozyme remained in the majority within the normal range or differed from the norm upward by 10-15%, with RSLT. the activity of lys ocyme was high and amounted to 24.44±5.71% and 29.57±6.8%, respectively. In the subjects assigned to group III, with primary and recurrent SLT, there was a decrease in the indicators of lysozyme activity below the norm within the range of 20-25%. This testifies in favor of the fact that the activity of lysozyme can be considered a marker not only of nonspecific reactivity, but also of the dysbiotic state of the mucous membranes of the upper respiratory tract. High numbers of lysozyme activity in children of group II make it possible to characterize a rather high level of adaptive capabilities of the body during colonization of the mucous membranes of the upper respiratory tract by gram-positive pathogenic flora (the presence of pathogenic gram-positive pathogens and their associations in the microflora of the upper respiratory tract is a stimulating factor for the production of lysozyme). In the surveyed group III, the low activity of salivary lysozyme is associated with the antilysozyme activity of the gram-negative flora, especially its intestinal representatives, and characterizes the severity of dysbiotic disorders.

Thus, the identification of complex associations of microorganisms, long-term persistence of pathogens in RSLT demonstrates a certain degree of dysbiotic disorders of the respiratory tract in this disease.

During OSLT, we noted an aggravation of the process of respiratory tract dysbiocenosis , characterized by the colonization of the respiratory tract mucosa, first by pathogenic gram-positive flora, then by the addition of gram-negative microflora, and even microorganisms that are unusual for this econiche.

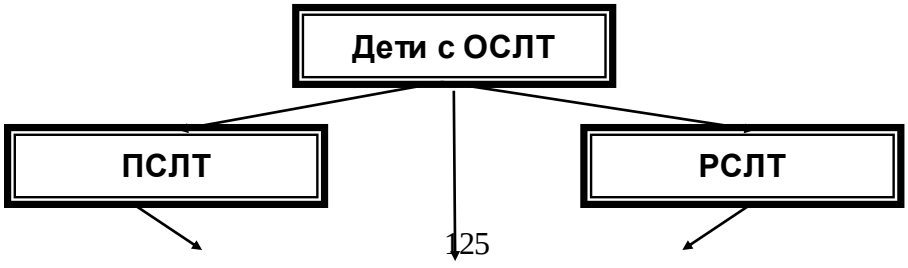
In children with varying degrees of severity of dysbiotic disorders of the upper respiratory tract, there was a difference in their clinical manifestations in primary and recurrent SLT . The level of severity of clinical symptoms in PSLT is quite high , but does not have significant differences depending on the degree of microbiocenosis disturbance , and in RSLT, clinical symptoms correlate with the degree of dysbiosis. With an increase in its degree, clinical manifestations intensify, thereby causing a deterioration in the condition of children.

CHAPTER VI . EVALUATION OF THE EFFICIENCY OF THE ALGORITHM OF COMPLEX TREATMENT AND PREVENTION OF CHILDREN WITH ACUTE STENOSING LAGINGOTRACHEITIS

6.1. Diagnosis and management tactics children with acute stenosing laryngotracheitis

Acute stenosing laryngotracheitis in children, which can cause life-threatening conditions in acute respiratory viral infections, remains a very urgent problem in otorhinolaryngological practice. This is due, first of all, to a violation of a vital function - breathing, due to the developing obstruction of the upper respiratory tract. Rapid determination of the etiology of acute respiratory viral infections is essential both for the prevention of nosocomial infections (by boxed placement of patients according to the etiological principle) and for the early appointment of etiotropic therapy. In addition to the above, deciphering the etiology of OSLT makes it possible to predict the further development of the disease, and in the case of the use of specific antiviral therapy, to reduce the duration of hospitalization and achieve complete recovery . At the same time, knowledge about the diagnostic capabilities of immunobiological preparations and OSLT diagnostic methods is of exceptional importance for choosing schemes and methods for using certain diagnostic tests and making recommendations for their further improvement.

Thus, summarizing the obtained results, we come to the conclusion that the diagnostic algorithm proposed by us, together with the results of laboratory methods, made it possible to make the correct diagnosis and choose the appropriate treatment option, the timeliness and adequacy of which made it possible to quickly stop the manifestations of stenosis and relapse of ASLT. This algorithm was used by us for a detailed examination of children (Fig. 6.1).



Rice. 6.1. Algorithm for diagnosing OSLT in examined children.

The tactics of managing sick children with acute stenosing lagingo-tracheitis is a very difficult problem.

Treatment of patients with acute laryngotracheitis should be divided as follows:

- organization of assistance; The best option is a specialized department based on a multidisciplinary hospital. Here, conditions are created for combining the efforts of otorhinolaryngologists, pediatricians, resuscitators, without which it is impossible to fully treat this contingent of children [Milkint KK, Sominina AA, Golovanova AK, 2003].;

- treatment of patients with acute laryngotracheitis depends on the stage of stenosis and is characterized by conservative therapy and / or intubation and tracheostomy,

- rehabilitation of children who have undergone prolonged intubation or tracheostomy.

Etiotropic treatment during acute laryngotracheitis includes the use of interferon and anti-influenza β-globulin. It is not advisable to prescribe antibiotics to a child whose acute laryngotracheitis proceeds according to the first clinical variant. The second clinical option involves the appointment of antibiotics for prophylactic purposes in an appropriate dose. The third clinical variant and an undulating course require intensive antibiotic therapy. With a continuous course, antibacterial drugs are prescribed according to the clinical variant.

When assisting patients in whom acute laryngotracheitis is accompanied by laryngeal stenosis in the stage of incomplete compensation, dexamethasone is used according to the standards, but this treatment is still used in the clinic. Intravenously injected: 10-20 ml of 20% glucose solution, 10% calcium chloride solution at the rate of 1 ml per year of life, 5% ascorbic acid solution at the rate of 1 ml per year of life, 2.4% solution of aminophylline at the rate of 0.2 ml per 1 кгbody weight, prednisolone solution 2-3 mg per 1 кгbody weight. Intramuscularly injected 1 ml of a 1% solution of diphenhydramine (or other antihistamine). Distracting procedures (hot foot baths, mustard plasters on the chest) and inhalations are effec-

tive. Antihistamines, antispasmodics and proteolytic enzymes are introduced into mixtures for inhalation.

The percentage of children hospitalized in the laryngology department is made up of patients with acute laryngotracheitis who develop decompensated stenosis of the larynx. Two stages of intensive care of such patients should be distinguished:

- prolonged intubation;
- tracheostomy.

Restoration of the lumen of the respiratory tract should begin with prolonged intubation, and if it is ineffective, perform a tracheostomy. For prolonged intubation, special thermoplastic tubes must be used. The child is then placed in an oxygen tent. Nutrition is carried out through natural routes. In the first days of intubation, the child is given antipsychotics. To prevent the formation of bedsores of the mucous membrane of the larynx, the tube must be changed daily. The ineffectiveness of prolonged intubation for 7-10 days is regarded as an indication for tracheostomy.

The following drugs were used as traditional therapy for children: Dexamethasone intramuscularly at a dose of 0.6 mg/kg of body weight, antibiotics, preferably cephalosporins intramuscularly at a dose of 0.05-0.1 mg/kg of body weight, antihistamine drug Suprastin in / m at a dose of 1 mg / kg of body weight, in the form of an aerosol, 1-2 doses 3-4 times a day or inhalations through a nebulizer, 1.25-2.5 mg with stenosis of 2-3 degrees, with an increase in body temperature Analgin 0.2-0.4 ml of a 25% solution per 10 кгbody weight + Diphenhydramine 12.5-25 mg IM as needed. In order to detoxify, a solution of calcium chloride 1% - 100.0 ml was injected intravenously, to eliminate bronchospasm, eufilin 2.4% -2.0 per 100.0 ml of physical saline was used. solution in / in drip.

Complex therapy was as follows: against the background of traditional therapy, the patient was injected with a nebulizer with a bacterial immunomodulator polyoxidonium in order to directly affect the mucous membrane of the larynx and

vocal folds and stimulate local immunity. Polyoxidonium powder was dissolved in 5 ml of 0.9% saline, inhalation of the polyoxidonium solution using a nebulizer was carried out for the first time for 5 minutes, and then 7-8 minutes every other day for 5 sessions. Polyoxidonium is effective when used simultaneously with traditional therapy. The drug enhances the effect of these drugs, which allows you to reduce the dose, shorten the course of treatment and significantly prolong remission.

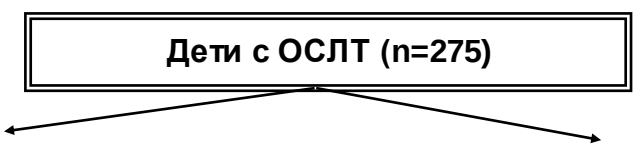
The immunomodulatory drug Derinat was prescribed at a dose of 0.5 ml per year of life, 1 time per day, No. 5, every other day 5 more injections every other day.

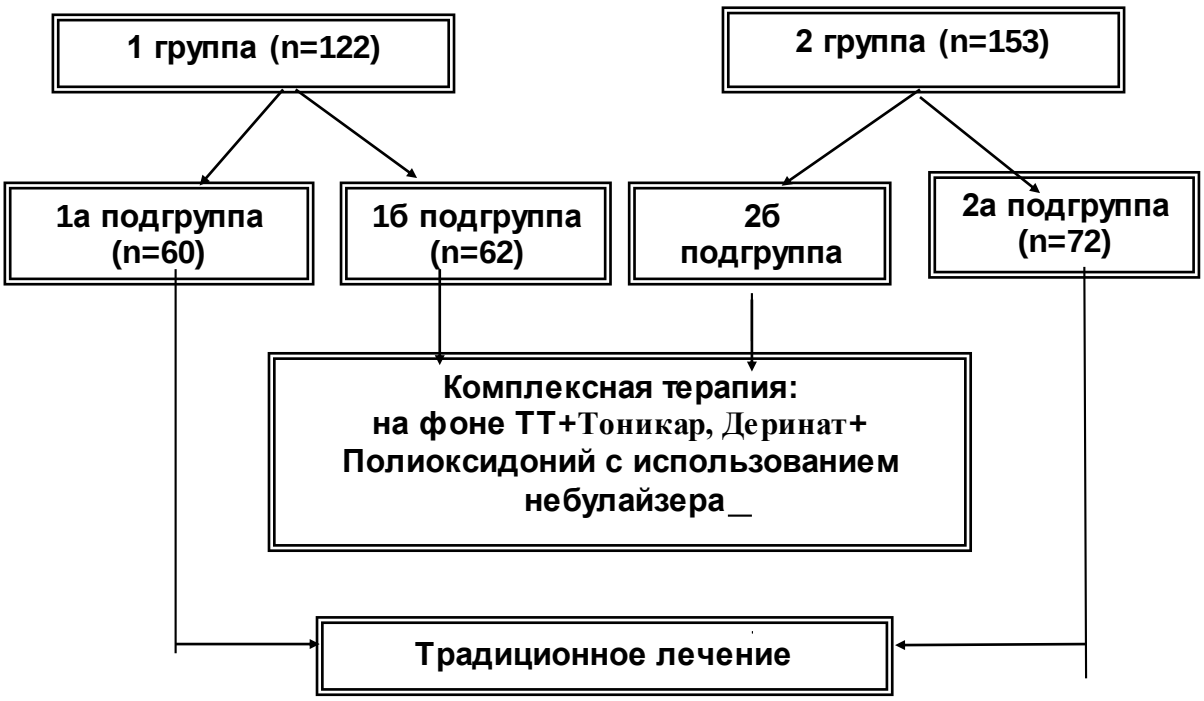
Derinat activates cellular and humoral immunity, optimizes specific reactions against fungal, viral and bacterial infections. The drug stimulates reparative and regenerative processes, normalizes the state of tissues and organs in dystrophies of vascular origin.

In addition, we prescribed the antioxidant drug Tonikar, 5 ml of a scoop with meals, the duration of the course was 10 days.

6.2. Evaluation of the effectiveness of complex treatment children with various forms of acute stenosing lagingotracheitis

The outcomes of OSLT are directly dependent on the severity of the disease and the timely initiation of complex therapy. OSLT treatment consists of - pathogenetic , symptomatic therapy and nonspecific hyposensitization. The commonality of the main pathogenetic mechanisms of the development of the disease in various forms of OSLT determines the universality of pathogenetic methods for their treatment.





Rice. 6.3. Algorithm for complex treatment of various forms of OSLT

Our studies show that the complex therapy developed by us gave a more pronounced positive clinical result than in subgroups where traditional therapy was used.

To adequately assess the effectiveness of the developed algorithm for managing children with various forms of OSLT, each group was divided into 2 subgroups.

Hoarseness or hoarseness, dry whistling rales for 6-7 days completely disappeared in all subgroups. The temperature dropped 3-4 days earlier. In the vast majority of cases (80.0%), the child's condition stabilized faster. According to the data obtained from the study, it is obvious that the use of complex therapy led to an improvement in the general condition of children in subgroups 1b and 2b (Table 6.1).

For the objectivity of assessing long-term results, we observed patients for 3 years after treatment. Patients were called for the first time for examination 4 weeks after discharge from the hospital and, depending on the patient's condition, were examined from 2 to 6 times a year. Relapses were observed at different times, for example, in 7 patients with RSLT who received TT: up to 3 months in 2

(1.6%), from 3 months to 1 year in 3 (2.4%), from 1 to 3 years in 2 (1.6%). After complex therapy, remission periods were longer and relapses were observed less frequently.

In recent years, it has been established that among the mechanisms of membrane damage in OSLT, the state of lipid peroxidation (LPO) processes, leading to the destruction of the phospholipid matrix of membranes and further cell necrosis, is important. A more pronounced increase in the intensity of LPO processes and suppression of the activity of AOP enzymes in the membrane structures of cells in children was observed in subgroups where complex treatment was used, indicating its effectiveness compared to traditional therapy. In principle, this happened, in all subgroups of the examined patients, the general reaction of the body to the process before treatment was an increase in the level of lipid peroxidation - high intensity of CL and MDA level, imbalance in the AOD system - low activity of SOD, CT and GR enzymes and high activity of GP in membranes erythrocytes.

In the subgroups where complex therapy was used, MDA significantly decreased after treatment with a high degree of significance ($P < 0.001$). In subgroup Ia in patients with PSLT against the background of complex therapy, the level of MDA decreased by 1.1 times, in Ib - 1.6, in 2a - 2, in 2b - 1.44 times. The remaining parameters after treatment were significantly ($P < 0.001$) reduced compared with the subgroup of patients treated with TT, but did not reach the normal level (Table 6.2).

Taking into account that disorders of the immune system play a decisive role in the mechanism of OSLT development, we studied the dynamics of cellular and humoral immunity in the examined children with OSLT before and after treatment.

When analyzing the immune parameters of children with PSLT of subgroup Ib after the use of complex therapy, 9 out of 10 studied parameters of cellular immunity were within the acceptable norm versus two after TT, which indicates a high immunocorrective effectiveness of complex therapy.

After complex therapy, the number of leukocytes significantly decreased by 50.6%, the absolute and percentage of total lymphocytes by 20.1%. The level of T-suppressors, which was overestimated before the start of treatment, increased by 21.4%, and T-helper levels decreased by 4 times.

And in the RSLT form, the picture was somewhat different in the subgroup where patients received TT, the indicators decreased significantly, but far from normal values, and in the subgroup where patients received complex therapy, the analysis of the immunogram indicates a statistically significant decrease in the level of leukocytes by 37.1% , lymphocytes - by 10.5%, the level of T-suppressors - by 64.5% and the level of T-helpers - decreased by 2.5 times ($P<0.001$) (Table 6.3).

An analysis of the parameters of the humoral link of the immune status of patients with PSLT showed that after the use of complex therapy, 4 out of 6 studied indicators of cellular immunity were within the acceptable norm against one after TT, which again confirms the high immunocorrective effectiveness of complex therapy.

The number of lymphocytes significantly decreased in children with PSLT of the Ia subgroup by 31.4%, in the Ib subgroup - by 46.0%, in children with RSLT of the 2a subgroup - by 19.5%, in the 2a subgroup - by 25.9%. There was a significant decrease in the level

immunoglobulins: the content of Ig A in children with PSLT of subgroup I a was 2.7 times, in subgroup I b - 2.8, in children with RSLT of subgroup 2a - 1.7, in subgroup 2a - 1.9. The content of Ig M and IgG in children with PSLT significantly decreased ($P<0.001$), in patients of subgroup Ib, the level of IgG reached the level of practically healthy people. In children with RSLT after treatment, the level of Ig M decreased insignificantly ($P>0.05$) (Table 6.4).

Thus, complex therapy has a positive effect on the immunological reactivity of OSLT patients, which contributes to an increase in the therapeutic effect.

However, these trends, even if they are statistically significant, do not provide complete information. More significant is the determination of the percentage of patients with transcendental changes in the values of immune status indicators, i.e. frequency analysis.

According to the results of frequency analysis after treatment with TT in patients of subgroup Ia with PSLT, a decrease in both T-lymphocytes from 92.3 to 63.1%, leukocytes from 84.6 to 23.1%, CD 4 from 96.9 to 72, 3%, CD 8 - from 90.8 to 84.6% at the level of the third degree of hyperfunction.

In the study of immunoglobulins, patients with hyperfunction of the 3rd degree were not identified, a significant decrease was found within the first and second degree. There was a transient deficiency of IgG immunoglobulins in 25.4% of patients (Table 6.5).

The rating algorithm after TT looked like: $CD8_{3}^{+}$ $CD4_{3}^{+}$ T-lymph $_{3}^{+}$ IgA_{1}^{-} IgM_{1}^{+} IgG_{2}^{+} lymph $_{1}^{+}$ lake $_{2}^{+}$.

After complex treatment in patients with PSLT, first-degree immune deficiency was mainly observed, which is not necessary to eliminate. The rating algorithm after complex therapy looked like: IgG_{1}^{-} IgM_{1}^{-} IgA_{1}^{-} lake $_{1}^{+}$ Lymph $_{1}^{-}$ T-lymph $_{3}^{-}$ $CD8_{3}^{-}$ $CD4_{3}^{-}$ (Table 6.6).

Analysis after treatment with TT in patients of the 2a subgroup of children with PSLT revealed a decrease in both T-lymphocytes from 78.8 to 32.7%, leukocytes from 61.5% to 0, CD 4 from 78.8 to 46.2%, CD 8 – from 84.6 to 30.8% at the level of the third degree of hyperfunction. The rating algorithm after TT looked like $CD4_{3}^{-}$ IgG_{1}^{+} IgA_{1}^{-} lake $_{2}^{+}$ IgM_{1}^{+} Lymph $_{2}^{-}$ T-lymph $_{2}^{+}$ $CD8_{3}^{+}$. (Table 6.7).

Thus, the rank assessment of TT and complex treatment of both PSLT and RSLT revealed the advantages of the latter.

When comparing the effectiveness of various types of therapies, it was found that complex therapy had a more pronounced immunocorrective effect on PSLT, then the targets were T-helpers, T-suppressors, immunoglobulins, and deep leukocytes, lymphocytes, T-lymphocytes.

An important factor in homeostasis disturbance is EI, which is caused by the accumulation of biologically active components in the blood as a result of activation of catabolic processes with a decrease in EI.

When assessing the severity of endogenous intoxication using a paramecium test, in children with PSLT after TT, a significant increase in the survival time of paramecia was found in the study of blood serum (PSLT - 16.2±0.21 and RSLT - 17.2±0.42 min) , and after complex therapy 18.1±0.50 min and 17.6±0.44, respectively. It is clearly defined here, RSLT, that the paramecium test did not reach the control, the results of treatment are somewhat worse, and with PSLT it almost reached the control values (Table 6.6).

We have studied the dynamics of LII in patients before and after treatment. Comparing the values of the Kalf-Kalif leukocyte intoxication index in subgroups treated with TT (PSLT - 3.1±0.09 and RSLT - 5.4±0.15) and in subgroups after complex treatment (PSLT - 1.08±0.03 and RSLT - 2.1±0.05). Thus, the data obtained characterize the high level of intensity of leukocyte reactions in patients before treatment, which is an additional criterion for assessing the severity.

A study of SMP in patients over time showed that during treatment, the level of SMP gradually decreased, which was accompanied by a clinical improvement in the patient's condition (Table 6.7).

To illustrate the results obtained, consider the following clinical examples:

Clinical example 1.

Extract from the medical history of patient V., 4 years old.

From the anamnesis of the disease: suffers from recurrent stenosing laryngotracheitis on the background of acute respiratory viral infections since 1 year of life, suffered 3 episodes of stenosis of the larynx against the background of acute respiratory viral infections. The disease always proceeds against the background of febrile temperature, pronounced catarrhal syndrome. Outpatient at the age of 3 years examined by an allergist, total immunoglobulin E was 58 IU/ml, allergic genesis of the disease excluded.

From the anamnesis of the disease: he fell ill in the morning on the day of hospitalization, the temperature rose to 38°C, abundant mucous discharge from the nose, coughing. The local pediatrician prescribed symptomatic therapy. Deterioration of the disease in the evening - against the background of persistent fever, the cough became "barking", the voice was hoarse, and shortness of breath appeared. According to the SMP, he was hospitalized in the infectious diseases department, where he was diagnosed with acute respiratory viral infections, stenosing laryngotracheitis of the 1st degree (recurrent).

A survey was carried out - bacteriological examination of the nasopharynx (CFU / swab) - Staphylococcus aureus (10^4), alpha-hemolytic streptococcus, saprophytic nesseria were isolated; oropharynx - Staphylococcus aureus (10^5), alpha-hemolytic streptococcus, pigment nesseria.

Diagnosed with dysbiosis of the mucous membranes of the upper respiratory tract I degree.

Complete blood count - hemoglobin 100 g / l, erythrocytes - 3.5 million, color index - 0.9, leukocytes - 5.8 g / l, eosinophils - 3, stab neutrophils - 2, segmented neutrophils - 45, lymphocytes - 44, monocytes - 6, ESR - 12 mm/hour.

The allergization index (AI) is 1.22 (the norm is 0.79-1.08 c.u.).

Leukocyte intoxication index (LII) - 0.94 (norm 0.3-1.5 c.u.).

Laboratory indicators: MDA - 7.14 nmol / ml; DC - 1.30 U / mg / lipids; NO_2^- (whole blood) - 0.055 mmol/l; NO_2^- (erythrocytes) - 0.24 mmol / l; hydroxyproline - 2.13 μg / ml; total immunoglobulin E - 98 IU / ml.

The child underwent a course of basic therapy. The course of therapy included: hypoallergenic diet, irrigation of the mucous membranes of the upper respiratory tract with mineral water 4 times a day, chest massage (10 procedures), breathing exercises, physiotherapy.

At the end of the rehabilitation activities, a survey was carried out.

Bacteriological examination of the nasopharynx (CFU/tampon) - isolated Staphylococcus aureus (10^3), alpha-hemolytic streptococcus; oropharynx - Staphylococcus aureus (10^4), alpha-hemolytic streptococcus, pigment nesseria.

Preservation of dysbiosis of the mucous membranes of the upper respiratory tract of the 1st degree was diagnosed.

Complete blood count - hemoglobin 126 g / l, erythrocytes - 3.4 million, color index - 0.9, leukocytes - 6.3 g / l, eosinophils - 3, stab neutrophils - 1, segmented neutrophils - 27, lymphocytes - 61, monocytes - 8, ESR - 8 mm/hour.

Allergization index (AI) - 2.55 (norm 0.79-1.08 c.u.).

Leukocyte intoxication index (LII) - 0.41 (norm 0.3-1.5 c.u.).

In the contents of the large intestine - the total number of Escherichia coli - 5.28 lg CFU / g (drastically reduced), there is hemolysin-producing E. coli - 9.87 lg CFU / g, Staphylococcus aureus - 4.77 lg CFU / g, fungi of the genus Candida - 5 35 lg CFU/g, the level of bifidobacteria was 8.90 lg CFU/g (reduced). Indicators of the function of external respiration (SPIROSIFT -3000, Japan) (% of the age norm): VC - 89%, FVC - 82%, FEV_1 - 87%, PSV - 80%, IT - 93%, $ISO_{25\%}$ - 84%, $MOS_{50\%}$ - 86%, $MOS_{75\%}$ - 90%, MVL - 77%.

Laboratory indicators: MDA - 6.92 nmol / ml; DC - 1.28 U/mg/ lipids; NO_2^- (whole blood) - 0.048 mmol/l; NO_2^- (erythrocytes) - 0.22 mmol / l; hydroxyproline - 4.21 μg / ml; total immunoglobulin E - 102.7 IU / ml.

Conclusion: after the therapy, the child retains symptoms of dysbiosis of the nasopharynx and oropharynx of the 1st degree (the titer of Staphylococcus aureus has decreased, but is diagnostically significant); indicators of the function of external respiration have improved, but some of them (PSV, MVL) are at the lower limit of the age norm, which indicates the lack of reserve capacity of the lungs; airway hypersensitivity persists; the allergization index increased, laboratory parameters remain elevated compared to those in healthy children.

After 9 months, this patient experienced the 5th episode of laryngeal stenosis against the background of SARS.

Clinical example 2.

Extract from the medical history of patient S., 5 years old.

From the anamnesis of the disease: suffers from recurrent stenosing laryngotracheitis against the background of SARS from the age of 2, suffered 5 episodes of stenosis of the larynx against the background of SARS. The disease always proceeds against the background of subfebrile temperature, pronounced catarrhal syndrome. The phenomena of stenosis of the larynx are stopped in a specialized infectious diseases department of respiratory viral infections during the first two days from the moment of hospitalization of the child.

From the anamnesis of the disease: he fell ill acutely, the temperature rose to 38.8°C, abundant mucous discharge from the nose, dry cough. Deterioration of the disease in the evening - against the background of persistent fever, the cough became "barking", the voice was hoarse, and shortness of breath appeared. According to the SMP, he was hospitalized in the infectious diseases department, where he was diagnosed with acute respiratory viral infections, stenosing laryngotracheitis of the II degree (recurrent).

Conducted examination - bacteriological examination of the nasopharynx (CFU / swab) - isolated Staphylococcus aureus (10^3), pneumococcus (10^5), alpha-hemolytic streptococcus; oropharynx - Staphylococcus aureus (10^6), hemolytic staphylococcus (10^4), alpha-hemolytic streptococcus, saprophytic nesseria.

Diagnosed with dysbiosis of the mucous membranes of the upper respiratory tract I degree.

Complete blood count - hemoglobin 118 g / l, erythrocytes - 3.3 million, color index - 0.9, leukocytes - 7.4 g / l, eosinophils - 3, stab neutrophils - 4, segmented neutrophils - 53, lymphocytes - 28 , monocytes - 12, ESR - 16 mm/hour.

Leukocyte intoxication index (LII) - 1.47 (norm 0.3 - 1.5 c.u.).

Threshold sensitivity of the airways with histamine, performed after 14 days - moderate threshold sensitivity (threshold concentration of histamine was 4 mg/ml).

Laboratory indicators: MDA - 7.50 nmol / ml; DC - 1.38 U / mg / lipids; NO_2^- (whole blood) - 0.065 mmol / l; NO_2^- (erythrocytes) - 0.25 mmol / l; hydroxyproline - 2.15 μg / ml; total immunoglobulin E - 228 IU / ml.

On the background of traditional therapy , a patient was injected with a bacterial immunomodulator polyoxidonium using a nebulizer in order to directly affect the mucous membrane of the larynx and vocal folds and stimulate local immunity. Polyoxidonium powder was dissolved in 5 ml of 0.9% saline, inhalation of the polyoxidonium solution using a nebulizer was carried out for the first time for 5 minutes, and then 7-8 minutes every other day for 5 sessions at the same time, and the immunomodulatory drug Derinat was administered at a dose of 0.5 ml per year of life 1 time per day, No. 5, every other day 5 more injections every other day. In addition, we prescribed the antioxidant drug Tivortin, 5 ml of a scoop with meals, the duration of the course was 10 days.

At the end of therapeutic measures, an examination was carried out.

Bacteriological examination of the nasopharynx (CFU / swab) - isolated alpha-hemolytic streptococcus, micrococci; oropharynx - alpha-hemolytic streptococcus, pigment nesseria, micrococci.

Diagnosed with the normal composition of the microflora of the mucous membranes of the upper respiratory tract.

Complete blood count - hemoglobin 124 g / l, erythrocytes - 3.5 million, color index - 0.9, leukocytes - 5.7 g / l, eosinophils - 0, stab neutrophils - 0, segmented neutrophils - 37, lymphocytes - 58, monocytes - 5, ESR - 7 mm/hour.

Leukocyte intoxication index (LII) - 0.59 (norm 0.3-1.5 c.u.).

Indicators of respiratory function (SPIROSIFT - 3000, Japan) (% of the age norm): VC - 99%, FVC - 95%, FEV_1 - 97%, PSV - 99%, IT - 98%, $ISO_{25\%}$ - 100%, $MOS_{50\%}$ - 99%, $MOC_{75\%}$ - 100%, MVL - 95%.

The threshold sensitivity of the airways with histamine is normal (the threshold concentration of histamine was 12 mg/ml).

Laboratory indicators: MDA - 5.65 nmol / ml; DC - 1.21 U/mg/lipids; NO_2^- (whole blood) - 0.040 mmol/l; NO_2^- (erythrocytes) - 0.21 mmol / l; hydroxyproline - 3.30 mcg / ml; total immunoglobulin E - 78 IU / ml.

Conclusion: after the 1st therapy program, the composition of the microflora of the mucous membranes of the upper respiratory tract normalized in the child; indicators of the function of external respiration within the age norm; normal airway sensitivity; the allergization index has increased, but it remains within the normal range; laboratory parameters are comparable with those in healthy children. During 28 months of observation of episodes of stenosis of the larynx against the background of acute respiratory viral infections, this child did not have.

6.3. Preventive measures to prevent PSLT disease and recurrence of RSLT

The basis for the prevention of OSLT in children, of course, is the formation of their own adequate immune response. Proper selection of the immune preparation is the key to the success of preventive measures in OSLT. We carried out prophylaxis in 2 stages in children with PSLT:

Stage 1 is carried out in the fall with the use of drugs: Genferon nasal spray by aerosol injection of 1 dose (50,000 IU) into each nasal passage 2 times a day for 5 days was used; drug Derinat / m 0.5 ml (7.5 mg) 1 time per day for 5 days; Stage 2 - the same drugs, doses and terms of application, but only in the spring.

For children with RSLT in the relapse-free period, for the purpose of prevention, we used Genferon nasal spray preparations by aerosol administration of 1 dose (50,000 IU) in each nasal passage 2 times a day for 5 days; drug Derinat / m 0.5 ml (7.5 mg) 1 time per day for 10 days; and at stage 2, the same preparations, doses and terms of application were used, but only in the spring.

In addition, prevention is facilitated by the optimization of lifestyle, including the establishment of a rational daily regimen, good nutrition, and environmental control.

Correction of the daily regimen in children with recurrent infections is aimed at eliminating activities and games that lead to overwork, overexcitation of the child, reducing stressful situations, and normalizing sleep.

As part of the ongoing complex of preventive measures, OSLT children need a balanced diet to reduce the frequency of relapses. It should be varied, containing an adequate amount of vitamins and minerals, taking into account the daily need of the child for proteins, fats and carbohydrates.

Recently, environmental control has been given a lot of attention in OSLT prevention programs. Prevention of frequent acute respiratory viral infections consists in reducing possible contacts with sources of infection in the family and preschool institutions, using anti-epidemic measures in the focus of infection, reducing the use of public transport, lengthening the time spent outdoors, controlling humidity and room temperature. In addition, frequent respiratory morbidity is closely associated with passive smoking, so smoking cessation in the family is an important condition for treatment and prevention.

Do not lose their relevance in the prevention of frequent relapses rinsing the throat with antiseptic decoctions of chamomile, St. John's wort, etc.; irrigation therapy: washing the nasal passages with saline solutions, as well as a variety of hardening programs.

Hardening is a system of measures aimed at increasing the stability of genetically predetermined defense mechanisms and adapting the body to many factors so that daily and seasonal, periodic and sudden changes in temperature, atmospheric pressure, etc. did not cause drastic changes in the growing organism. Hardening is based on the training of vasomotor mechanisms for an adequate response to cold exposure. Systematic contrast air or water hardening is accompanied by an increase in the body's resistance to temperature fluctuations in the environment and

an increase in the immunological reactivity of the body. The adaptive abilities of the child lend themselves well to training. The use of any methods of hardening improves the operation of the thermoregulatory apparatus and expands the possibilities of adapting the body to changing temperature conditions. Hardening does not require very low temperatures, the contrast of exposure and the systematic nature of the procedures are important. They harden well the impact on the soles of the feet and gradually - on the entire skin of the trunk and extremities. The maximum duration of hardening procedures should not exceed 10-20 minutes, its regularity and gradualness are much more important. Hardening procedures are well combined with gymnastics and chest massage.

6.4. Mathematical assessment of the risk of recurrence of acute stenosing laryngotracheitis from the point of view of evidence-based medicine

The practical significance of predicting the development of relapses of acute stenosing laryngotracheitis is to determine the risk factors for the development of relapses of OSLT. To this end, we used multivariate statistical analysis.

In the process of developing an algorithm for predicting risk factors for the development of OSLT relapses, we identified 3 tasks:

- development of the direction of the search for "main" prognostic factors;
- determination of quantitative risk assessments based on the results of studying a combination of factors;
- study of the structure of relationships between various prognostic factors.

Among the factors that determine the development of OSLT, many researchers distinguish fetal-maternal, somatic, anamnestic, immunological. As you know, risk factors for a child include a burdened obstetric history of the mother, somatic diseases. Not every factor carries significant information for a probable prognosis of the formation of fetal infection.

We evaluated the prognostic significance of each of the identified 47 risk factors, mathematically identified in the detailed collection of anamnestic data of 40 children and 74 children with OSLT. The method of individual forecasting was taken as a basis (Ushakova G. A. et al., 1982). And the degree of informativeness of the factor was assessed by the method of Bayes et al. (1991) and the assessment of each factor in points, set on the basis of the calculation of the prognostic coefficient, made it possible to compile a "Prognostic risk map for the development of OSLT".

The essence of the method is to determine the risk indicators of binary features - risk factors. If there are two possible values - "the attribute is present" and "the attribute is absent", there are also two risk indicators - for i =1 or i =2. Let us denote the probability (and relative frequency) of the presence of a trait in healthy children through p , in patients - q . Then for newborns who have this factor, we obtain the expression of the risk coefficient according to the formula:

$$L = \frac{q}{p}$$

For children who do not have a risk factor, the risk ratio is

$$M = \frac{1-q}{1-p}$$

You can, of course, use percentages instead of probabilities.

$$L = \frac{q}{p}$$

$$M = \frac{100-q}{100-p}$$

The risk factor L and M logically complement each other. If the presence of this feature is a risk factor (L >1), then its absence is an anti-risk factor (M<1) and vice versa.

Along with the risk coefficient, the so-called risk indicator is also used, which is equal to the ratio of the risk coefficient of a disease in children with a sign, and a similar coefficient for a child who does not have that sign:

$$R = \frac{L}{M} = \frac{q(1-p)}{p(1-q)} = \frac{q(100-p)}{p(100-q)}$$

From a mathematical point of view, the use of the coefficient L and M is more preferable than R . Indicators L and M have a clear probable meaning, more fully characterize the patient.

On the other hand, the indicator R is more compact, since it characterizes the significance of the feature with only one number, and not two (like L and M).

A burdened premorbid background is a risk factor for the development of OSLT diseases, especially allergic diseases (R = 12.62), bronchopulmonary (R = 7.18), lung disease (R = 2.34), cardiovascular diseases (R = 4 .47), gastrointestinal disease (R = 4.20) (Table 5.6).

Table 6.7

Prognostic criteria for a burdened hereditary history

No.	Risk factors	L	M	R
one	Allergic diseases	10.01	0.94	12.62
2	Bronchopulmonary diseases	9.97	0.93	11.18
3	kidney disease	4.25	0.95	4.47
four	Thyroid disease	1.52	0.74	2.06
5	*Cardiovascular diseases*	4.25	0.95	4.47
6	lung disease	1.99	0.85	2.34
7	Gastrointestinal disease	3.81	0.91	4.20
eight	Viral hepatitis	1.88	0.69	2.72

The pathological course of childbirth was observed in almost all children, among the diseases stood out asphyxia during childbirth, which is due to the presence of cardiovascular disease (R = 4.47) in mothers of the examined children (Table 6.7).

Table 6.8

Prognostic criteria for complications at birth of the examined children

	Risk factors	L	M	R
one	Pathological course of childbirth	1.01	0.84	1.19
2	Long dry period	9.04	0.74	13.41
3	Asphyxia during childbirth	10.56	0.68	15.44
four	prenatal dystrophy	1.95	0.51	3.82
5	Chronic intrauterine hypoxia	1.72	0.70	2.45
6	Atelectasis	4.37	0.75	6.84

To the risk criteria in children born with a long anhydrous period in their mothers (R = 13.41), atelectasis (R = 6.84) (Table 5.8).

All past and infectious diseases in the neonatal period affect the development of OSLT

Table 5.8

Prognostic criteria diseases of the examined children in the neonatal period

	Risk factors	L	M	R
3	parainfluenza virus	10.54	0.70	15.06
four	flu virus	12.50	0.93	13.44
5	Respiratory distress syndrome	6.86	0.90	7.62
6	Artificial feeding from birth	19.85	0.55	36.09
7	RS virus	9.72	0.79	12.30
eight	Adenovirus	24.05	0.63	38.17
9	Viral-bacterial etiology	22.1	0.92	42.50

and infectious diseases during pregnancy are of great importance (Table 5.9).

Table 5.9

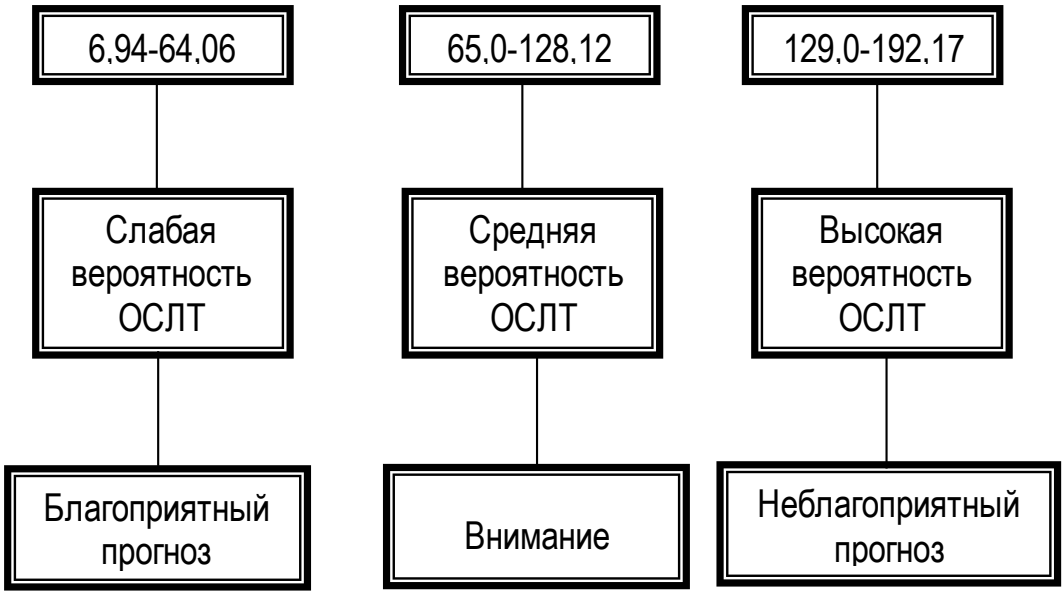
Prognostic criteria and infectious diseases during pregnancy

	Risk factors	L	M	R

one	SARS	3.17	0.63	5.00
2	Angina	3.38	0.88	3.83
3	Gestational pyelonephritis	8.44	0.88	9.60
four	Acute bronchitis	2.29	0.91	2.52
5	Pneumonia	5.94	0.92	6.46

The most significant in predicting the development of ASLT are infectious diseases of the mother during pregnancy, aggravated somatic history, artificial feeding from the moment of birth, infectious diseases in the neonatal period.

The value of the ranges and groups of individual forecasts for the development of OSLT



Rice. 6.3. Range values and individual forecast groups risk of developing OSLT

The probability that the child will not get sick occurs when the total risk index lies in the range from 6.94 to 64.06. In the range of 65.0-128.12 risk index, the probability of the disease is average. But in the range of 129.0-192.17, the probability of developing OSLT is maximum.

Thus, on the basis of a clinical and statistical study, the developed "Prognostic Map" made it possible to quantify the likelihood of OSLT development. with various combinations of risk factors. Simple and accessible work with the "Prognostic card" will allow it to be widely used in the diagnosis of OSLT , which will help to identify the early risk of developing OSLT and the timely use of corrective therapy.

Thus, complex therapy has a positive effect on the immunological reactivity of children with ASLT, on the general condition of children, which contributes to an increase in the therapeutic effect.

Timely prevention can reduce and prevent the risk of developing laryngotracheitis and prevent relapses of RSLT.

CONCLUSION

The analysis of literature data showed that a significant proportion of children with repeated episodes of laryngotracheitis have background allergic diseases (atopic dermatitis, allergic rhinitis, bronchial asthma) [Veltishchev Yu.E. , 200 6; Karaulov A.V., Klimov E.V., 2001; Mironov A. Yu., Savitskaya K. I., Vorobyov A. A., 2001; Ryvkin A.I., Bedinskaya N.S., Orlova S.N., 2005; Stazhadze L.L., Spiridonova E.A., Feklisova L.V., Lobushkova I.P., 2009; Tatochenko V.K., Dorokhova N.F., Shmakova S.G., 2006]. However, despite the fact that in the etiology of OSLT, especially recurrent, infectious and non-infectious factors, in particular allergic ones, are important, the diagnosis of the latter has so far been covered only fragmentarily [Drannik GN, 2003; Popovich , A. M. _ , 2004; Stazhadze L.L., Spiridonova E.A., Feklisova L.V., Lobushkova I.P., 2009].

The study is based on a clinical and laboratory examination of 275 children with acute stenosing laryngotracheitis, who were under observation and admitted to the city infectious diseases hospital No. 3 from 2011 to 2013.

The inclusion criteria for the survey were:

- age from 6 months to 7 years;
- acute and recurrent forms of stenosing laryngotracheitis;
- parental consent to the participation of the child in the study.

For an adequate assessment of the data of laboratory studies, 40 practically healthy children of a comparable age were examined.

All examined children were divided into 2 groups according to the forms of acute stenosing laryngotracheitis according to the classification of Yu.V. Mitina (1986):

- 1 group of 122 (44.4%) children with primary stenosing laryngotracheitis.
- Group 2 - out of 153 (55.6%) recurrent stenosing laryngotracheitis.

An analysis of the distribution of children with acute stenosing laryngotracheitis by gender showed that boys are more likely to get sick than girls. The ratio of

girls and boys was 1:1.8 in group 1 in group 2 - 1:1.7 OSLT develops more often in young children (from 6 months to 3 years). In group 1, the majority of children (60.7%) fell ill at the age of 1 to 3 years, and at the age of up to one year, 16.4% of children fell ill and in the period from 3 years and older - 23.0%, in group 2 the picture is somewhat different: the incidence at the age of 3 years and older is almost 3 times higher than in group 1.

This is due to the anatomical and physiological features characteristic of this age group - a relatively narrow lumen of the larynx, looseness of the submucosal layer in the subglottic space, abundant vascularization of the mucous membrane of the respiratory tract, and increased vascular permeability.

In history, almost all children had ARVI, the percentage of exudative catarrhal diathesis was also high (71.3% and 69.9%, respectively, in groups), hyperthermic syndrome was observed in 53 (43.4%) children of group 1 and in 33 (21 .6%) - 2 groups. The index of past diseases in group 1 was 3.6, in the main group - 3.0, which indicates the relationship between the incidence of past diseases and the development of OSLT.

An analysis of concomitant diseases in children with acute stenosing laryngotracheitis showed that all children had OSLT against the background of acute respiratory viral infections, and such diseases as rhinitis, tonsillitis, anemia and, less often, otitis media, aggravated the condition of sick children. In 2 (1.6%) children of the 1st group and in 7 (4.6%) of the 2nd group, febrile convulsions developed against the background of high temperature. Almost a third of sick children were accompanied by bronchitis, pneumonia. A burdened premorbid background provokes the development of OSLT. Among the most dangerous complications inherent in acute respiratory viral infections, in terms of frequency, severity of manifestations, difficulties and urgency of solving therapeutic problems, acute stenosing laryngitis occupies a special place.

Patients were mainly admitted to the hospital on the 1-2 and 3-4 days of illness. At the same time, in the group with recurrent laryngotracheitis, none of the

patients was admitted later than 4 days from the onset of the disease, which is apparently due to the alertness that arises in parents in the event of a relapse of the disease.

Spicy stenosing laryngotracheitis belongs to the group multifactorial diseases. Its formation is based on the interaction endogenous and exogenous factors.

Unfavorable course of ante-, intra - and neonatal periods and the presence of allergic reactions in early childhood are considered factors influencing the formation of a child's health.

An analysis of hereditary history showed that a special place is occupied by the aggravation of his allergic (in group 1 - 49 (40.2%), in group 2 - 59 (38.6%)) and broncho-pulmonary diseases of relatives in the first and second line (in group 1 - 45 (36.9%), in group 2 - 62 (40.5%)).

The foregoing indicates the great importance of the role of allergic reactions in the genesis of primary and recurrent forms of OSLT, and that the development of relapses is facilitated by the hyperreactivity of the upper respiratory tract and the allergic mood of the child's body.

The average age of onset of the first episode of laryngeal stenosis in children with acute respiratory viral infections corresponds to the age interval from 1 to 6 years.

An analysis of the premorbid background of children with this pathology did not reveal significant differences in children with primary and recurrent SLT, which allows us to consider them as stages of a long-term disease.

Primary SLT was observed in 26 (21.3%) under the age of 1 year, from 1 to 3 years - in 53 (43.4%), from 3 to 6 years - in 43 (35.2%).

37 (24.2%) children with RSLT underwent SLT for the first time at the age of 1 year, in the period from 1 to 3 years - 64 (41.8%), from up to 6 years - 52 (34.0%).

Once a year, a relapse was observed in 39 (25.5%), in 8 (5.2%) - 1 time in a year and a half, most often - 82 (53.6%) - 3 times a year and more often 3 times a year. year at 24 (15.7%).

Analysis of the length of time between the first and repeated SLT showed that after 1 month in 18 (11.8%) cases there was a relapse, in 19 (12.4%) - after 2-4 months. The overwhelming number of relapses recurred after 4-8 months in 27 (17.6%) cases and after 1-2 years - in (19.0%), and more than 2 years - in 42 (27.5%) cases.

An analysis of the respiratory history also showed that 46 (30.1%) children had no viral and bacterial diseases between 1 and repeated episodes of SLT, 20 (13.1%) had 1 case of ARVI, 22 (14.4%) patients - 2 cases, 38 (24.8%) - from 3 to 5, and 27 (17.6%) - more than 5 cases of ARVI, i.e. 42.7% of children had three and more SARS (which were not accompanied by laryngeal stenosis syndrome) between the first and repeated SLT.

During the clinical examination of the majority of children admitted to the hospital during the acute period of laryngeal stenosis, pronounced symptoms of intoxication, including high body temperature, were noted in children with PSLT in 79 (64.8%) hospitalized children, and in children with RSLT - in 51 (33 .3%). Catarrhal syndrome in the form of conjunctivitis, nasal congestion, nasopharyngitis was observed in 96 (75.2%) children with recurrent SLT ($P<0.001$) and in 103 (84.4%) with primary.

A physical examination in the lungs with RSLT revealed no changes in 27 (17.6%) children, dry wheezing rales were heard in 21 (13.7%), wet rales of various sizes - in 35 (22.9%) ($P<0.001$) . During PSLT, auscultatory changes in the lungs were not observed in 27 (17.6%) children, dry whistling rales were detected in 48 (39.8%) children, wet rales of various sizes - also in 10 (8.2%) children.

An analysis of the frequency of symptoms of respiratory failure in the examined children showed that they occur much more often in children with RSLT than in children with PSLT, which indicates their weakened condition. inspiratory

shortness of breath in children with RSLT by 79.3% (P<0.001), noisy breathing - 2.1 times, retraction of compliant chest areas - 2.9 times more often than in children with PSLT.

The duration of stenosis of the larynx was up to 1 day with RSLT - 88 (57.5%), up to 3 days - 51 (33.6%), more than 3 days - 15 (9.8%); with PSLT, respectively 50 (41%), 56 (45.9%), 16 (13.1%)

When assessing the severity of OSLT by degrees, we considered three - components:

- the presence of symptoms of laryngitis in the form of a change in the timbre of the voice (hoarseness or hoarseness) and cough (rough "barking" or rough wet);

- the presence of symptoms of stenosis: inspiratory dyspnea, noisy breathing, retraction of pliable places of the chest (jugular supra- and subclavian fossa, intercostal spaces and epigastric areas);

- the presence of symptoms of respiratory failure: inspiratory shortness of breath, pallor of the skin, cyanosis of the nasolabial triangle , acrocyanosis, general cyanosis, tachycardia, participation of auxiliary muscles in the act of breathing (swelling of the wings of the nose, tension of the muscles of the neck, participation in the act of breathing of the intercostal muscles).

The severity of croup syndrome in the children we observed was set on the basis of clinical data:

OSLT I degree **was observed in 30 (24.6%) children with PSLT and in 26 (17.0%) - RSLT.**

II degree was observed in 80 (65.6%) children with PSLT and in 104 (68.0%) children with RSLT, the general anxiety of the patient.

III degree stenosis **was observed in 12 (9.8%) children with PSLT and in 23 (15.0%) children with RSLT.**

At the IV degree of stenosis, a sphyxia occurs. At present, it is practically not found. None of the children we observed had

The vast majority of patients were admitted to the hospital with a clinic OSLT syndrome II degree. The development of croup syndrome up to degree III was noted only in isolated cases, mainly in children with a recurrent course of the disease.

All patients presented with severe symptoms. intoxication in the form of subfebrile and febrile temperature, headache , weakness, loss of appetite, up to its absence. Significant differences in the manifestation of intoxication syndrome in groups of patients with ALT and RLT we have not identified.

All the children observed by us had typical clinical symptoms of ASLT, in the form of: voice changes (hoarseness, hoarseness, up to aphonia), rough, dry unproductive ("barking") cough.

The seasonality of the disease is traced, exacerbations are observed more often in winter, autumn, autumn-winter. No significant difference is noted. The role of the external environment (climate, season of the year) and its pollution in the development of OCLT is noted in the literature [Belousov Yu.B., Karpov M.V., Leonova M.V., Efremenkov O.V. , 2006 ; Sukhovetskaya V.F., Sominina A.A., Drinevsky V.P., Milkint K.K. , 2004 ; Tarasov D.I., Ababii I.I. , 2004], but there is no analysis of the consequences of their combined impact on pathogenesis stenosis.

Thus, the analysis of the premorbid background of children suffering from ASLT makes it possible to identify the main risk factors for the development of the disease: repeated acute respiratory viral infections, allergic diseases, aggravated hereditary, obstetric anamnesis.

According to the literature, the main link in the pathogenesis of functional changes in organs and systems in OSLT in children is the development of respiratory failure, manifested by a disorder of external, pulmonary and tissue respiration, hypoxia and hypoxemia. Under the influence of hypoxia and hypercapnia, the functional state of the central nervous system and the neuro-reflex regulation of the vital functions of the body are disturbed. As a result of impaired functions of the most important organs and systems in the body, changes in metabolism occur. Vio-

lation of gas exchange and redox processes, hypoxia and hypoxemia lead to the activation of anaerobic oxidation of underoxidized metabolic products. Under the influence of hypoxia, bacterial toxins, products of impaired metabolism and changes in hemodynamics in children with OSLT, there are violations of the function of vital organs. These changes are accompanied by an increase in the activity of LPO processes and a restructuring of the antioxidant defense systems of erythrocytes.

It is possible that in these violations of the micro - and macrorheological properties of blood, a significant role belongs to the activation of free-radical processes. So, E. V. Roitman, I. I. Dementieva (2002) showed that the activation of free radical processes in erythrocytes reduces the fluidity and deformability of erythrocyte membranes, disrupts the morphological structure of erythrocytes and thereby changes the aggregation ability of these cells.

Activation of lipid peroxidation and AOS, as a result of this, the presence of changes in the lipid structure are the basis for the implementation of therapeutic and preventive measures aimed at correcting these disorders

In the pathogenesis of acute stenosing laryngotracheitis, great importance is attached to the role of specific and nonspecific factors of immune protection. Literature data indicate that OSLT reveals significant changes in the cellular link of immunity, which are expressed in a decrease in the total content of T-lymphocytes. The state of humoral immunity is characterized by disimmunoglobulinemia . At the same time, most researchers note a decrease in Ig A and Ig G in combination with an increased level of Ig M. A downward trend in Ig M occurs mainly in uncomplicated ASLT [Burton D. _ M. , Seid A. _ B. , Kearns D. _ B. , 2002; Deitmer T. , 2007; Fonseca S. V., Irisi S. , 2009].

The main component of regulation in the immune system is the interaction of T- and B-class lymphocytes and their subpopulations. Obviously, the pathological process in PSLT and RSLT was accompanied by compensatory stimulation of the cellular mechanisms of the immune system.

As can be seen from the analysis of the results obtained, there is a significant increase in T-helpers ($P<0.001$) in patients with PSLT, and with RSLT it did not differ much from the control values.

In addition, the absolute number of T-suppressors, as well as the percentage, was statistically significantly increased in patients of group 1 ($P<0.001$), and in patients of group 2 it decreased compared to control values.

With PSLT and RSLT, IRI increased by 1.6 and 1.9 times, respectively, which indicates the development of autoimmune processes in the body /

According to the literature, in an inflammatory reaction, to a greater extent due to the action of an infectious agent and to a lesser extent - in atopic inflammation, IFN-γ, activating the macrophage link of immunity, is a direct inducer of the synthesis of IL-1β [Masek V ., Sorli J. , Kopriva S. , Marin J. , 2004; Wyatt J. , 2012]. Under physiological conditions, IL-1β is able to enhance the production of IFN-γ by activating Th1 cells.

The conducted correlation analysis made it possible to establish the presence of a direct relationship between the content of IFN-γ and IL-1β in the blood serum. We found that the strength of this bond is inversely proportional to the shape of the OSLT. So, if in the control group the correlation coefficient was close to unity ($r=0.95$), then in groups 1 and 2, the values of the correlation coefficient were 0.59 and 0.37, respectively. Significant correlation coefficients between other pairs of cytokine levels were not obtained in any group.

Therefore, the results of our study confirm the existence of a relationship between the concentrations of IFN-γ and IL-1β, and this dependence is direct and decreases depending on the form of OSLT, which indicates violations of immunoregulatory mechanisms.

Therefore, a reduced serum concentration of INF-γ indicates a violation of IL-1β - mediated production of IFN-γ by Th-1 cells.

Thus, it was found that the majority of children with OSLT have a reduced content of T-cells. A low content of CD3+ cells indicates a reduction in the pool of

circulating T-lymphocytes and, therefore, a possible risk of their insufficiency when an intensive immune response is needed. A decrease in the content of functionally active T cells naturally affects the content of specialized phenotypes that perform helper and suppressor functions.

Undoubtedly, a decrease or increase in their number can have a negative impact and, in all likelihood, is one of the pathogenetic factors of the inflammatory process. As is known, NK cells play an important role in anti-infective protection, and their changes in both directions are apparently due to several reasons: partial immunodeficiency, insufficient production of non-toxic antibodies that block the activity of immunocompetent cells.

One of the causes of immunodeficiency states is a violation in the body under the influence of various agents of immunoregulatory processes carried out with the help of Th1- and Th2-helpers. As is known, the former synthesize cytokines that stimulate cellular immunity (IL-1β, IL-2, IL-6, IL-8, IL-12, INF, TNF, etc.), the latter synthesize cytokines that stimulate humoral immunity (IL-4 , IL-5, IL-10, transforming growth factor - IL-1 β, etc.). In a normally functioning organism, there is a certain balance of interaction between Th-1 and Th-2 helpers. But a strong change in their activity under the influence of any influence can lead to serious adverse consequences in the functioning of the immune system as a whole.

It has been established that the allergic process causes the activation of Th2 helpers and the synthesis of cytokines that have a suppressive effect on cellular immunity. The cytotoxic mechanism of damage is switched on, which is associated with T-killers [Wyatt J. , 2012].

More and more convincing evidence is accumulating that the increased incidence and severity of ASLT in children depend on the reactivity of the child, and a change in the specific and nonspecific reactivity of the homeostasis defense systems is the first and main condition for the development of the infectious process. In this regard, our next task was to study the effect of endogenous intoxication on the immunological reactivity of young children with OSLT.

The results of studies of the immune system depending on the degree of intoxication in OSLT patients in young children are presented. When analyzing the immunological parameters, it was found that all children during the peak of the disease showed a significant decrease in the content of leukocytes, the absolute number of lymphocytes, T-lymphocytes, T-helpers ($P<0.05-<0.001$) and a significant increase in the levels of T-suppressors (DM_8) and T-killers (DM_{16}), compared with the healthy group ($P<0.001$). An imbalance in the subpopulation composition of T-lymphocytes, namely, a decrease in DM_4 and an increase in DM_8 indicate a sharp decrease in immunological reactivity and a direct dependence on the degree of endogenous intoxication.

One of the levels of anti-infective protection in OSLT is the phagocytic system. In healthy children, the phagocytic activity of neutrophils (PAN) was in the range of 55.2±1.6%. In the acute period of the disease, it was noted that the FAN index in OSLT was lower than in healthy children ($P<0.001$) for all degrees of endogenous intoxication. Another important peripheral population in children is B-lymphocytes. In healthy children, an average of 27.5±1.4% of B-lymphocytes circulate in the peripheral blood. With OSLT, the relative and absolute number of B-lymphocytes during the peak period significantly differs from their number in healthy children ($P<0.05-<0.001$) in the direction of decrease.

Dysimmunoglobulinemia was observed in children with ASLT in the acute period of the disease. Immunoglobulin IgG, IgA and IgM were significantly reduced, at all degrees of intoxication ($P<0.001$), in direct proportion to the severity of the clinical picture.

So, during the peak period, at stages I and II of intoxication, IgG production was 1.4 times, and at stage III it was 2.2 times reduced, compared with healthy children. The concentration of serum IgA in patients was significantly reduced compared with the data of the healthy group with I and II degrees of intoxication ($P<0.001$), and with III degree of intoxication it was 116.8±17.8 mg% versus 130±8.6 mg% ($P>0.05$). The concentration of IgM in patients was significantly

reduced compared to the data of the healthy group with II and III degrees of intoxication from 1.3 to 1.4 times (P<0.001), and with I degree of intoxication it was 108±7.2 mg% versus 115.2 ± 8.2 mg% (P >0.05). These indicators indicate a reduced antimicrobial immunity and a decrease in the antitoxic properties of the body. Thus, the observed sample can be characterized as a sample with significant metabolic and immune status disorders, pronounced fluctuations of the studied parameters.

The conducted studies showed an inversely proportional dependence of the vast majority of immunological parameters (T-lymphocytes r=-0.88 (P<0.01), and their subpopulations; T-helpers - r=-0.24; (P<0.05), IgG r=-0.66 (P<0.01) on the severity of the degree of endogenous intoxication in patients with OSLT in young children.

An analysis of our own studies of SMPs in patients with OSLT in young children once again confirmed the literature data that among the first toxic properties of SMPs is their participation in the development of secondary immunosuppression, the ability to influence the blast transformation reaction in the presence of phytogenaglutinin (PGA). Under the action of SMF, the intensity of blast transformation of lymphocytes decreases, rosette formation is inhibited, and the reaction "graft versus host" occurs. SMP inhibit the proliferation of fibroblasts, the phagocytic activity of neutrophils and the rate of their migration, cause impaired platelet function [Ermachenko M.F., 2010; Zaitseva O.V., 2006].

Thus, the conducted immunological studies in the midst of OSLT in children indicate the development of immunological deficiency, both cellular and humoral. An inversely proportional dependence of indicators on the degree of endogenous intoxication was revealed.

Summarizing the presented data, it should be noted that allergic diseases are a very urgent problem already because of their high prevalence. And the noted systemic and local immunological changes can be qualified as a secondary immunodeficiency state.

The microflora of the respiratory tract in our studies was assessed during primary and recurrent SLT in the acute period (from days 1 to 5 of illness) and during remission (from day 6 of illness).

The microbial landscape was assessed at the first stenosis of the larynx and at its recurrence against the background of acute respiratory viral infections in the acute period (from the 1st to the 7th day of illness) before the start of antibiotic therapy and in the period of full health (at least 10-14 days after the respiratory viral and / or bacterial infection). Not only the qualitative microbiological landscape was taken into account, but also its quantitative content.

In the acute period of viral infection, only 87 (31.6%) children in the nasopharynx and 52 (18.1%) children in the oropharynx had a normal microflora composition.

Dysbiotic processes were characterized by the colonization of the mucous membranes of the upper respiratory tract by pathogenic and conditionally pathogenic gram-positive and gram-negative flora, a decrease in the release of saprophytic and normal microflora. Undoubted leadership in this process has Staphylococcus aureus. It occurs both in the form of a monoculture and in the form of associations - in combination with other pathogenic pathogens. Along with gram-positive bacteria, fungi of the genus *Candida were detected* , as well as *Klebsiella, E. coli, Enterobacter, Moraxella* , which formed complex associations.

We analyzed the composition of the microbiocenosis of the respiratory tract depending on the number of episodes of laryngeal stenosis on the background of a viral infection. In patients with 3 episodes of stenosing laryngotracheitis (SLT), the normal composition of the microflora of the nasopharynx was recorded in 136 (49.4%) of the examined children, in the oropharynx - in 82 (29.8%). In other cases, gram-positive bacteria were most often detected in 91 (33.1%) in the nasopharynx and in 85 (30.1%) in the oropharynx and Staphylococcus aureus in monoculture (45 (16.3%) and 86 (31.3%)), that is, microbial communities were formed that characterize the I degree of dysbiosis. Associations of gram-positive with

gram-negative microbes (II degree of dysbiosis) were rare - in 18 (6.5%) cases in the nasopharynx and in 27 (9.8%) - in the oropharynx.

In children with 4-5 cases of stenosis of the larynx in the acute period of viral infection, normal microflora in the upper respiratory tract was determined in a third of patients. The pathogenic flora of the nasopharynx in the acute period is mainly represented by associations of gram-positive bacteria 158 (57.5%), a monoculture of Staphylococcus aureus is quite often found - in 81 (29.5%) cases. Complex associations of microorganisms were registered in 29 (10.5%) children. In the oropharynx of these patients, the composition of the microbiocenosis changes somewhat - the proportion of gram-positive flora 102 (37.1%) and the monoculture of staphylococcus 22 (8.0%) decreases, the number of patients with complex associations of microbes increases significantly - up to 112 (40.7 %), gram-negative microorganisms that are unusual for this econiche appear in monoculture - in 29 (10.5%) of the examined. In the period of convalescence of acute respiratory viral infections, microbiocenosis is represented in the nasopharynx mainly by Staphylococcus aureus in monoculture in 162 (58.9%), there are almost no complex associations -15 (5.5%). In the oropharynx, complex associations were more often recorded; 98 (35.6%) percent of children with S. aureus on the mucous membranes in monoculture remains high.

In children with 6 or more episodes of SLT against the background of ARVI, the normal composition of the microflora in the period of acute infection was determined in the nasopharynx in 45 (16.4%) of the examined patients and in 29 (10.5%) - in the oropharynx, in the period of convalescence in 55 (20.0%) and 42 (15.3%) respectively. Dysbiotic disorders in the nasopharynx in the acute period were expressed by an increase in the proportion of children with complex associations of microbes 75 (27.3%), and the preservation of the leading role of gram-positive flora 112 (40.7%). In the oropharynx, there is a significant (12.5%) growth of allochthonous flora - *E. coli, Enterobacter, Moraxella* , fungi of the genus *Candida* and their associations with gram-positive microbes 121 (44.0%) with a de-

creasing role of gram-positive pathogens 72 (26.2%) . In the period of convalescence in the nasopharynx of these children, gram-negative microorganisms also began to be detected in a monoculture 17 (6.2%), the percentage of gram-positive microbes 34 (12.4%) decreases, there is a significant increase in Staphylococcus aureus and complex associations of bacteria by 42%. In the oropharynx, the microflora is represented by complex associations - in 125 (45.5%) children, a decrease in the role of gram-positive microbes and an increase in the percentage of allochthonous flora to 6.7%.

lysozyme activity in children with primary and recurrent SLT in the acute period and in remission was also considered as a marker of the severity of respiratory tract dysbiocenosis. In the acute period with PSLT, the activity of salivary lysozyme corresponded to the standard values (from 17 to 25%). During the period of remission, activity indicators decrease slightly, but in most cases they constitute the lower limit of the norm. With RSLT in the acute period of the disease, very high numbers of lysozyme activity are detected, exceeding the norm by 1.5-2 times, and during remission with RSLT, the lowest indicators are recorded , which also differ from normal by 1.5-2 times.

When analyzing the activity of lysozyme depending on age, it was found that in children from 0 to 3 years old, the activity of lysozyme in the acute period is the lower limit of the norm, it decreases during remission, in most cases 1/2 of the normative indicator. With RSLT in the acute period of the disease in all age periods, salivary lysozyme exceeds the standard value by 5-10%, and during the period of remission, the lowest activity of lysozyme was also noted in children from 0 to 3 years old, at 3-6 years old it corresponds to the norm and decreases in older children by 5-10% of the norm.

The level of salivary lysozyme activity during SLT depends on the period of the disease. Lysozyme, as a marker of the state of nonspecific reactivity of the organism, during the period of remission can indirectly characterize the state of the - microbiocenosis of the mucous membranes of the upper respiratory tract, since in

the presence of pathogenic and conditionally pathogenic microflora in the respiratory tract, which has antilysozyme activity, the level of lysozyme during this period can be very low. High, 2-3 times higher than normal, the level of lysozyme during remission indicates foci of chronic inflammation in the body, especially ENT organs that require sanitation and are in a state of active inflammation at the time of the examination.

In the acute period of the disease, an increase in the activity of lysozyme also indicates a microbiological problem, since with a high degree of dysbiosis, lysozyme is compensatory increased due to the production of the macrophage system and other blood cells involved in the inflammatory process. A decrease in lysozyme during the acute period of the disease is prognostically unfavorable, as it indicates a low immunological reactivity of the organism, including nonspecific protective factors.

We have analyzed changes in salivary lysozyme activity during the acute period of SLT, depending on the degree of dysbiotic disorders of the upper respiratory tract, i.e., in children of groups I, II, and III (Table 13). In children of group I, the activity of salivary lysozyme during PSLT remained in the majority within the normal range or differed from the norm upwards by 10–15%, while during RSLT it also remained within the normal range. In children of group II with primary and recurrent SLT, lysozyme activity was high and amounted to 24.44±5.71% and 29.57±6.8%, respectively. In the subjects assigned to group III, with primary and recurrent SLT, there was a decrease in the indicators of lysozyme activity below the norm within the range of 20-25%. This testifies in favor of the fact that lysozyme activity can be considered as a marker not only of nonspecific reactivity , but also of the dysbiotic state of the mucous membranes of the upper respiratory tract. The high figures of lysozyme activity in children of group II make it possible to - characterize a rather high level of adaptive capabilities of the organism during colonization of the mucous membranes of the upper respiratory tract by gram-positive pathogenic flora (the presence of pathogenic gram-positive pathogens and their as-

sociations in the microflora of the upper respiratory tract is a stimulating factor for the production of lysozyme). In the surveyed group III, the low activity of salivary lysozyme is associated with the antilysozyme activity of the gram-negative flora, especially its intestinal representatives, and characterizes the severity of dysbiotic disorders.

Thus, the identification of complex associations of microorganisms, the long-term persistence of "aggressive" pathogens in RSLT demonstrates a certain "maturity" of dysbiotic disorders of the respiratory tract in this disease.

During OSLT, we noted an aggravation of the process of respiratory tract dysbiocenosis , characterized by the colonization of the respiratory tract mucosa, first by pathogenic gram-positive flora, then by the addition of gram-negative microflora, and even microorganisms that are unusual for this econiche.

The tactics of managing sick children with acute stenosing laryngotracheitis is a very difficult problem.

Treatment of patients with acute laryngotracheitis should be divided as follows:

- organization of assistance;
- treatment of patients with acute laryngotracheitis, which is accompanied by stenosis of the larynx in the stage of compensation and incomplete compensation;
- intensive care of patients with acute laryngotracheitis, which is accompanied by stenosis of the larynx at the stage of transition from incomplete compensation to decompensation;
- intensive care of patients with acute laryngotracheitis in the stage of decompensation (prolonged intubation and tracheostomy);
- rehabilitation of children who have undergone prolonged intubation or tracheostomy.

The best option for the organizational form of assistance to such patients is a specialized department based on a multidisciplinary hospital. Here, conditions are

created for combining the efforts of otorhinolaryngologists, pediatricians, resuscitators, without which it is impossible to fully treat this contingent of children.

The main pathogenetic mechanisms that form respiratory disorders: swelling of the mucous membrane of the larynx and trachea, spasm of the muscles of the larynx , trachea and bronchi, hypersecretion of the glands of the mucous membrane of the larynx, trachea and bronchi, become the leading ones that determine the clinic, and ultimately therapy.

Complex therapy was as follows: against the background of traditional therapy, the patient was injected with a bacterial immunomodulator polyoxidonium using a nebulizer in order to directly affect the mucous membrane of the larynx and vocal folds and stimulate local immunity. Polyoxidonium powder was dissolved in 5 ml of 0.9% saline, inhalation of the polyoxidonium solution using a nebulizer was carried out for the first time for 5 minutes, and then 7-8 minutes every other day, 5 sessions at the same time, and instead of Anaferon for children, it was administered the immunomodulatory drug Derinat was prescribed at a dose of 0.5 ml per year of life 1 time per day, No. 5, every other day 5 more injections every other day. In addition, we prescribed the antioxidant drug Tivortin, 5 ml of a scoop with meals, the duration of the course was 10 days. The developed algorithm of complex treatment, as shown by the analysis of the obtained results, had a more pronounced clinical effect: hoarseness, hoarseness, wet rales of various sizes stopped, dry wheezing completely disappeared on days 6-7 in all subgroups.

For the objectivity of assessing long-term results, we observed patients for 3 years after treatment. Patients were called for the first time for examination 4 weeks after discharge from the hospital and, depending on the patient's condition, were examined from 2 to 6 times a year.

Relapses were observed at different times, for example, in 7 patients with RSLT who received TT: up to 3 months in 2 (1.6%), from 3 months to 1 year in 3 (2.4%), from 1 to 3 years in 2 (1.6%). After complex therapy, remission periods were longer and relapses were observed less frequently.

Recurrent stenosing laryngotracheitis belongs to the group of multifactorial diseases. Its formation occurs on the basis of the interaction of endogenous and exogenous factors, among which the most important are: unfavorable course of the ante-, intra- and neonatal periods, early infection, repeated viral and bacterial diseases and the presence of allergic reactions in early childhood. All preventive measures are aimed at overcoming these risk factors leading to such a serious illness in children.

CONCLUSIONS

1. The prevailing conditions for the development of acute laryngotracheitis , creating an unfavorable premorbid background, are maternal health, aggravated obstetric anamnesis, pregnancy complications , anemia, pathological childbirth, prematurity, artificial feeding , exudative-catarrhal and thymic-lymphatic diathesis, complication of the neonatal period infectious diseases and respiratory distress syndrome. The occurrence of acute laryngotracheitis in children is most often associated with parainfluenza infection (55.5% of cases) and other respiratory viral infections (up to 84.1%).

2. The presence of complex associations of microorganisms, long-term - persistence of pathogens in OSLT demonstrate a certain degree of dysbiotic disorders of the respiratory tract in this disease. During OSLT, there is an aggravation of the process of respiratory tract dysbiocenosis, characterized by the colonization of the respiratory tract mucosa, first by pathogenic gram-positive flora, then by the addition of gram- negative microflora and even microorganisms that are not characteristic of this econiche.

3. A common immunological pattern for OSLT is the suppression of - indicators of cellular and activation of humoral links and mmu nitet . PSLT in children is characterized by an increase in the level of B-lymphocytes and hyperproduction of IgA, IgG and IgE, as well as IL-4. The level of cytokines in the secretion of the oral cavity - IL-1β, TNFα and IL-4 in children with RSLT is sharply increased ($p<0.001$). The peculiarity of the immune status in RSLT is manifested by a long-term selective deficiency of IgA, including in combination with a high level of IgE, a decrease in phagocytosis, and an increase in the concentration - of CEC.

4. In patients with PSLT, a rating algorithm of disorders of the immune system was calculated, which makes it possible to identify key indicators of hypo- and r and perfunction of the immune system in terms of immunity: in patients with

PSLT, IgA_{2}^{-} IgM_{1}^{+} $CD8_{1}^{-}$ IgG_{1}^{-} $CD16_{1}^{+}$ $CD3_{1}^{+}$ $lymph_{3}^{-}$ $CD4_{3}^{+}$ $leuk_{2}^{+}$, in patients with RSLT: IgG_{2}^{-} IgA_{2}^{-} IgM_{1}^{+} $CD4_{1}^{-}$ $CD8_{2}^{-}$ $lymph_{3}^{+}$ $CD3_{1}^{+}$ $leuk_{2}^{+}$ $CD16_{1}^{+}$.

5. Violation of gas exchange, hypoxia and hypoxemia lead to an increase in the activity of lipid peroxidation processes and the restructuring of the antioxidant defense systems of erythrocytes. In children with RSLT, the level of indicators of endogenous intoxication is directly proportional to the severity of the course of the disease, only the level of these indicators is much higher than in children with PSLT .

6. The developed algorithms for the diagnosis and treatment of OSLT in 97.5% of patients with PSLT and in 86.3% of children with RSLT who received complex therapy made it possible to obtain a positive therapeutic effect, which, on average, reduced the length of stay in a hospital bed by 3 days. Observation of patients for 3 years showed that the developed method of treatment made it possible to prevent relapses of the disease, to lengthen the remission period.

7. In acute stenosing laryngotracheitis, preventive treatment is indicated according to the algorithm developed by us, which reduces the number of relapses of acute stenosing laryngotracheitis by an average of 3-4 times, reduces the length of stay of sick children in the hospital by an average of 3.5 bed-days, and therefore , expenditures of the state budget allocated for the treatment of children are reduced.

8. The developed "Prognostic map" allows to quantify the probability of OSLT development with various combinations of risk factors. The probability that the child will not get sick occurs when the total risk score is in the range from 6.94 to 64.06. In the range of 65.0-128.12 of the total risk index, the probability of the disease is average. But in the range of the total risk index of 129.0-192.17 , the - probability of developing OSLT is maximum.

PRACTICAL RECOMMENDATIONS

The conducted studies allowed us to recommend the following algorithm of measures when a child with ASLT is admitted to the hospital :

1. Assessment of anamnestic data, specifying the frequency of occurrence of JIT episodes and the presence of an allergic pathology in history.

2. Evaluation of clinical and laboratory parameters: clarification of the features of the clinical picture of the disease, interpretation of the results of a general blood test, virological, bacteriological.

3. Inclusion in traditional therapy of immunocorrective drugs with antiviral action of Derinat drugs intramuscularly, 0.5 ml 1 time per day for 5 days, the immunomodulatory drug Polyoxidonium is locally applied through a nebulizer, and the antioxidant drug Tonikar, 5 ml each. 2 times a day for a month.

4. In order to prevent relapses in sick children who underwent PSLT, prophylaxis should be carried out in 2 stages:

- Stage 1 should be carried out in the fall with the use of drugs: Genferon nasal spray by aerosol injection of 1 dose (50,000 IU) into each nasal passage 2 times a day for 5 days; drug Derinat / m 0.5 ml (7.5 mg) 1 time per day for 5 days;

- Stage 2, we recommend using the same preparations, doses, but only in the spring.

For children with RSLT in the relapse-free period, as a preventive measure, we recommend using Genferon nasal spray by aerosol administration of 1 dose (50,000 IU) in each nasal passage 2 times a day for 5 days; drug Derinat / m 0.5 ml (7.5 mg) 1 time per day for 10 days; and at stage 2, use the same preparations, doses only in the spring.

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