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MEDICINE AND PHARMACY

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Modern Aspects of Scleroma Clinical Manifestations and Diagnostics According to the Ukrainian Scleromic Center Data (Bibliographical Review & Own Experience)

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Abstract.
The presented analysis of literature data and own observations based on the Ukrainian Scleroma Center is devoted to the dynamics of prevalence, modern features of clinical manifestations and course, classification, future methods of primary chronic specific respiratory tract infection (scleroma), which is etiologically associated with Klebsiella

rhinoscleromatis verification. The impact of the introduction of the polymerization chain reaction for the verification of scleroma on the dynamics of its prevalence and clinical course is also predicted.

Keywords:
scleroma
rhinoscleroma
Klebsiella rhinoscleromatis
Infiltrates
airway stenosis
scleroma symptoms
course, prevalence

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According to Alexander Kitsera's research [11], "scleroma of the external nose, the so-called rhinoscleroma, described by the Ukrainian professor of surgery V.O. Karavayev, and only later - by the Viennese dermatologist Ferdinand Gebra" in 1870 (fig. 1).

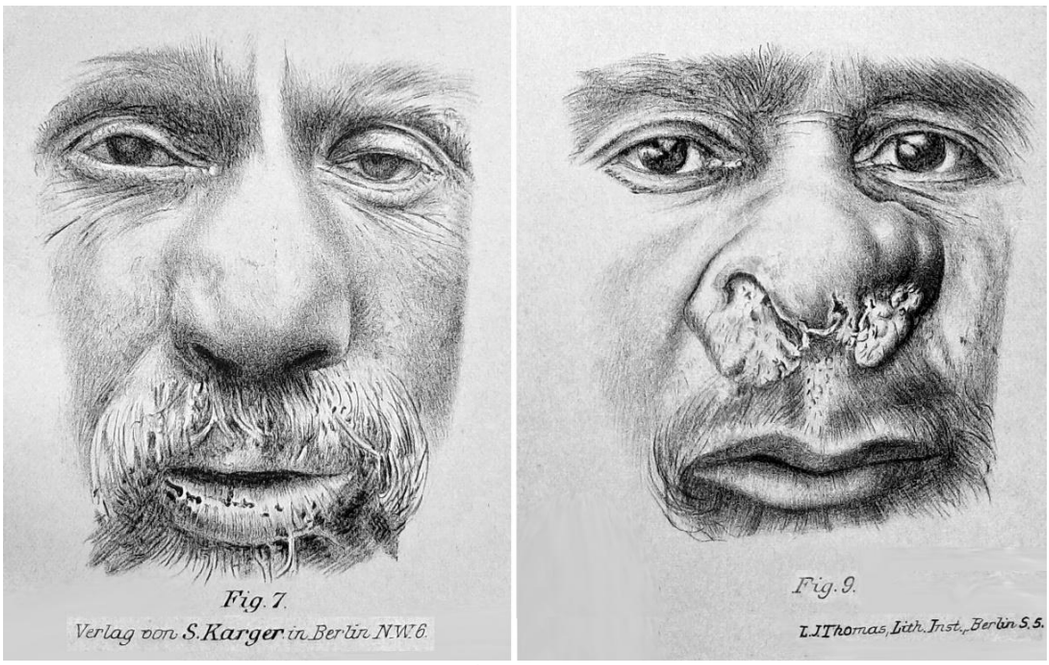

Figure 1

Photograph of a drawing from the 1902 P.H.Gerber atlas (Von Privatdocent Dr. P.H.Gerber. Atlas der Krankheiten der Nase, ihrer Nebenhöhlen und des Nasenrachenraumes. 363 Figuren auf tafeln. Berlin, Verlag Von S. Karger. Karlshtrasse, 15)

Scleroma is a primarily chronic infectious disease of the respiratory tract with low contagiousness caused by Klebsiella rhinoscleromatis and manifested by the formation of specific scleromatic granuloms (fig. 2, 3, 4, 5), which is transform into scar in the course of the disease (fig. 6, 8, 11, 12). Their location in the narrowest parts of the airways leads to stenosis. In addition, it can lead to facial deformation, dysfunction of the surrounding organs [28], and atrophy of the mucous membrane of the upper respiratory tract (fig. 7). Prolonged hypoxia and intoxication cause secondary

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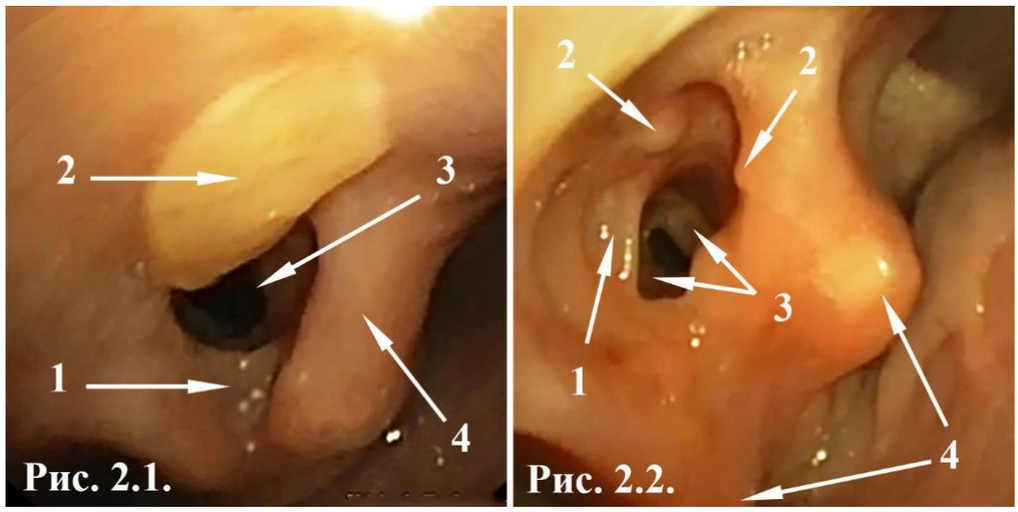
changes in most organs and systems of the body [2, 8, 10, 11].



Figure

2.1. Scarred crescentic membrane of the laryngeal vocal folds (1), epiglottis laryngeal surface granuloms (2) in a patient with scleroma which is complicated with subcompensated laryngeal stenosis. 3 – space of the larynx. 4 - aryepiglottical fold;
2.2. Left-sided cicatricial crescentic membrane of the laryngeal vestibular floor (1), small granuloms up to 3 mm in size (2), scarred concentric narrowing of the vocal folds (3) in a patient with scleroma. 4 – corniculate tubercles. Clinically subcompensated laryngeal stenosis

Prevalence of scleroma. Despite the publication of articles about scleroma in the PLOS (Public Library of Science) journal with open access – Neglected Tropical Diseases, this disease is not included in the list of so-called "forgotten" (neglected) diseases [30, 34] and continues to be detected in many countries [25, 32, 33, 35, 36, 38, 39, 41, 42]. The prevalence of scleroma is influenced by various economic, social and migration processes. There is even a certain increase in the number of scleroma patients in the developed countries such as the United States and France [27], mainly due to people emigrating from other regions [3, 26, 27, 31, 40]. Most publications analyze scleroma cases with unfavorable course or complications: in Mali [35], Chile [36], China [42], Poland [39], India [41], Morocco [33], Saudi

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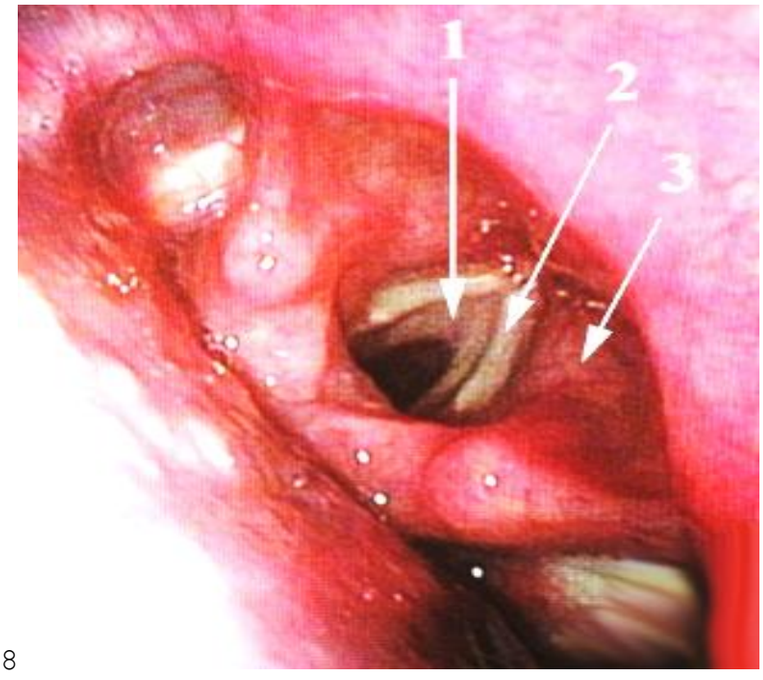
Arabia and Bahrain [32], Tunisia [25], Brazil [38] and other countries.

Some regions of Ukraine remain endemic foci of scleroma [1, 2, 8, 10, 11, 13, 17, 19, 20, 21]. The endemicity of scleroma is in some way related to hereditary factors that affect the onset and course of the disease [5, 11, 37]. However, a number of social, economic, and migration factors, as well as the use of modern antibacterial drugs, have led to certain changes in the prevalence of scleroma [13, 31, 40], its clinical course and the treatments effectiveness.



8

Figure 3

Pathologic laryngeal subglottic "folds" (1) as a result of specific scleromatic infiltration of the subglottic laryngeal floor in a patient with scleroma, which is complicated with subcompensated laryngeal stenosis; 2 - vocal fold; 3 - vestibular fold

Despite the reorganization of health care in Ukraine over the past decades, the Ukrainian Scleroma Center, which was founded in 1980 by order № 282 of the Ministry of Health of the USSR of 29.04.1980.1992, continue operates on the ENT-clinic of the Vinnytsia Regional Clinical Hospital named after

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M.I. Pirogov.

Over the past 5 years (2020-2024), 225 hospitalizations of patients with scleroma have been registered at the Ukrainian Scleroma Center, all from the regions of Ukraine (fig. 6). No hospitalizations were registered from the Autonomous Republic of Crimea and neighboring countries, as in previous decades. With a consistent downward trend in the incidence of scleroma and a slight decrease in hospitalization rates in time the COVID-19 pandemic and Russia's full-scale aggression against Ukraine, there is an increase in the percentage of hospitalizations of newly diagnosed cases of scleroma with an unfavorable course [12].

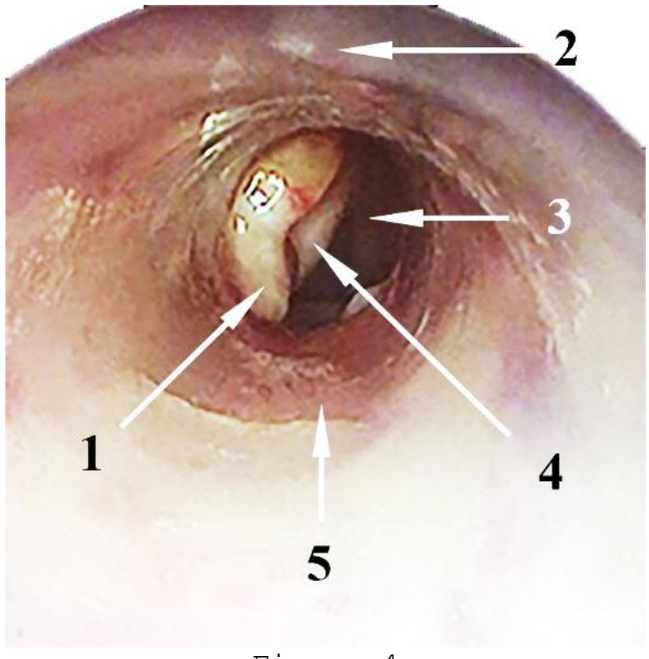

Figure 4

Pathologic laryngeal subglottic folds ("rolls") - due to specific infiltration of the subglottic region mucous membrane (1) in a patient with scleroma with a tracheostomy (view from the trachea through a T-shaped silicone stent (2, 5); 3 - space of the larynges; 4 - right vocal fold

Relevance. However, no universal methods of the space of airway stenosis restoring present, effective methods of curing upscleroma have not been found, and there are no ways

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to restore atrophied mucous membranes of the airways. Of course, it is hoped that timely diagnosis and adequate treatment of scleroma will, first of all, prevent airway stenosis and irreversible atrophy of the mucous membranes [8, 9, 15].

It is important to note that Klebsiella Rhinoscleromatis, which is etiopathogenetically associated with the onset and development of scleromatic infection and causes its unfavorable clinical course and insufficient treatment effectiveness, belongs to the multiantibiotic-resistant strains of Klebsiella pneumonia [24]. This is one of the factors that complicate the treatment of scleroma [7, 8, 9].

The latent course of scleroma can last for years, that is why most patients with scleroma seek help with airway stenosis or complications caused by the spread of specific infiltration to the skin of the external nose or into paranasal sinuses, orbit [8, 12, 18]. Also there have been cases of primary tracheal scleroma [22, 33, 36, 39].

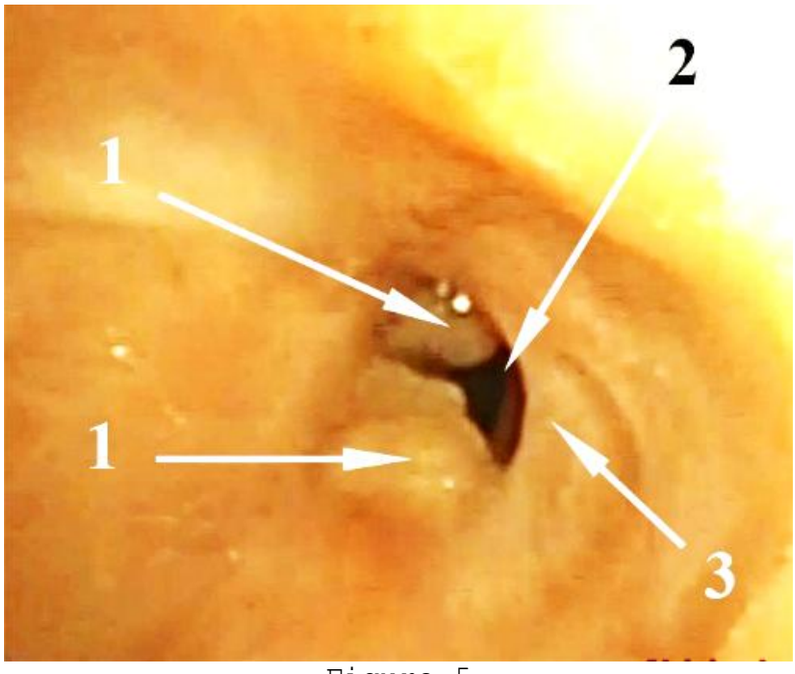

Figure 5

Infiltrates (1) and crescentic scar (3) of the middle third of the trachea in a patient with scleroma; 2 - tracheal space

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The next fundamental chain in the pathogenesis of scleroma after bacterial intoxication is hypoxia, which is caused by productive specific infiltration of the airways mucous membrane with subsequent scarring, which is most common in narrow places, therefore quickly causing their stenosis. Impaired external lung ventilation causes depression of tissue respiration with subsequent disruption of metabolic processes in most organs and systems of the body (arterial hypoxemia and hypercapnia, increased levels of residual nitrogen in the blood, impaired protein and water-electrolyte metabolism, adrenal cortex hypofunction, etc. [4, 6, 8, 9, 12, 14, 23, 33, 36, 39].

The diagnosis and treatment of patients with scleroma have naturally changed in accordance with the development of bacteriology, pharmacology, clinical immunology, as well as the technological development of surgical otorhinolaryngology.

Figure 6

Scarring deformity of the soft palate arch, "absence" of the uvulae due to scar dislocation into the nasopharyngeal space in a patient with scleroma

Diagnosis of scleroma. Scleroma can be suspected in patients with complaints characteristic of chronic inflammatory diseases of the respiratory tract with impaired

laryngeal or nasal breathing, swallowing, voice formation, and pronounced dystrophic changes in the mucous membranes of the respiratory tract. The clinical manifestations of scleroma manifest in three pathomorphologic processes: specific infiltration of the respiratory tract mucosa in the form of granulomas; their scarring in the absence of ulceration; dystrophy of the airway mucous membranes [2, 8, 10, 11]. However, with each new exacerbation of the disease, these processes are cyclically repeated. Therefore, sometimes in one area they are observed simultaneously, but in different combinations, which complicates their interpretation [2, 8, 10, 11].

The classic clinical signs of rhinoscleroma – "hard nose" with widespread specific infiltration and facial deformity, which were observed and demonstrated by Ukrainian researchers L.A. Zaritsky (1948), K.P. Derepa (1966), R.A. Barylyak and N.A. Sahelashvili (1974), O. Kitsera (1996), are practically not found today (fig. 10).

Clinical signs that allow to suspect scleroma are: prolonged painless and without ulceration infiltration with next scarring deformation of the columella and of the external nose alae with nostrils stenosis (fig. 8); granulomas, scars or crusts in the nasal cavity, concentric stenosis of the choanae; infiltration of the palatine arch and soft palate with their deformation, dislocation of the uvulae into the nasopharyngeal space with stenosis of the nasopharyngeal entrance (fig. 6, 11), but without complete atresia (fig. 11); stenosisof the laryngeal vestibulum due to infiltration and scar deformation of the aryepiglotical, interarytenoideal folds and epiglottis (fig. 2), vocal space stenosis (fig. 12) with restricted mobility of the vocal folds, new pathological subglottic folds due to symmetrical infiltration of the subglottic laryngeal floor with stenosis (fig. 3, 4), tracheal granulomas (fig. 5) or tracheal mucous membrain diffuse infiltration, single flat scars or scarred tracheal membranes, granulomas of the main bronchi with thickening of the carina, viscous mucus, greenish crusts (fig. 7) with a nauseating-sweet odor in the nasal cavity, pharynx, trachea against the background of atrophy of the airway mucosa [2, 8, 11, 15].

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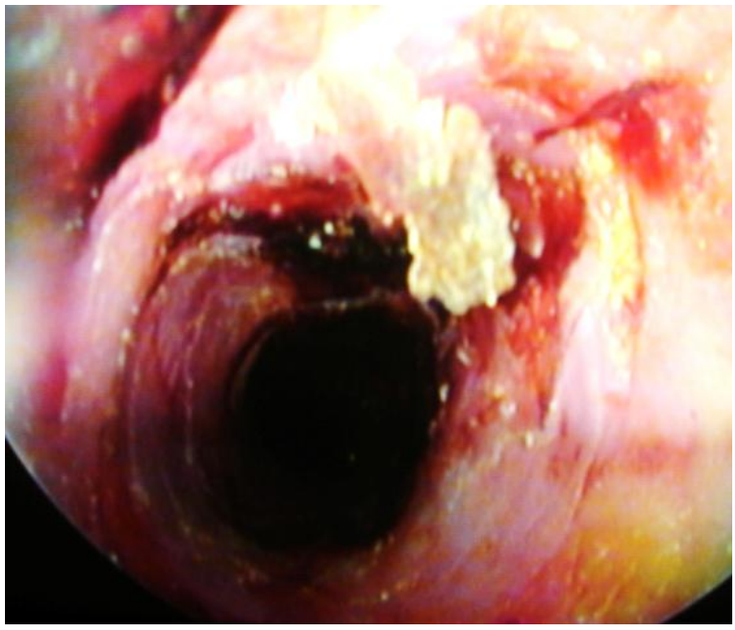

Figure 7
Hyperemia, mucosal thinning, viscous mucus and tracheal crusts in a patient with atrophic scleroma

As mentioned above, three pathomorphologic processes (specific infiltration, scarring of infiltrates and atrophy of the airway mucosa [2, 8, 10, 11, 29]) may occur simultaneously in scleroma, which complicates the interpretation of the classification of the scleroma stage and, accordingly, its treatment. For example, in the presence of scarring deformity of the soft palate and palatine arches, scarring dislocation of the uvulae into the nasopharyngeal space, there is a specific infiltration of the laryngeal subglottic space with stenosis. In this case, according to the clinical classification of K.P. Derepa (1966), the infiltrative form of scleroma is predominantly determined.

If "fresh" infiltrates appear against the background of atrophy of the airway mucosa, then the course can also be interpreted as a predominantly infiltrative form of scleroma.

If flat scars are observed against the background of atrophy of the airway mucosa, which do not cause stenosis or cosmetic deformation of the nose, and the patient is primarily concerned about dryness, cough, viscous mucus, crusts,

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unpleasant odor, and treatment of atrophy of the airway mucosa is necessary, then the atrophic form of scleroma is predominantly stated.

Figure 8
Scarring deformity with atresia of the nasal columella and alaes due to scleroma

Of course, in the presence of stenosis of scarring origin and the absence of infiltrates against the background of atrophy of the airway mucosa, the patient is diagnosed with a predominantly scarred form of scleroma. Undoubtedly, these options for combining different stages of the morphological and, accordingly, clinical course of scleroma should be taken into account when choosing rational tactics for treating scleroma in a particular case.

Methods of scleroma verification. In the presence of clinical (endoscopic) signs similar to scleroma, well-known methods of verification are used: bacteriological, histological and immunological.

Of course, bacteriologic examination could be the most common verification method, however, its informative value is at the level of 30-50% [2, 8, 10, 11]. One of the reasons for the low informational content of bacteriologic examination in

scleroma is the peculiarities of obtaining material for the study. Mucous membranes, which in most cases have been previously sanitized with antiseptics, do not contain the bacteria. The Klebsiella rhinoscleromatis is located in the submucosal layer and inside vacuoles of Mikulich cells in the specific infiltrates. Therefore, the scleroma bacteria can be obtained by a microbiological loop when infiltrates or mucous membrane under crusts are destroyed [2, 8, 10, 11]. In case of scarring of infiltrates, the informativeness of bacteriological examination decreases [10].

Figure 9

Geographical prevalence of scleroma patients hospitalized at the UkrainianScleroma Center (Vinnytsia) in 2020-2024

The informativeness of the pathohistological method is high in the presence of "fresh" infiltrates, in which large "foamy" Mikulich cells are identified, in the vacuoles of which there are paired rhinoscleroma bacteria in various stages of incomplete determination, plasma cells with protoplasmic basophilia and an eccentrically located nucleus with chromatin in the periphery. In the process of infiltrates scarring, the concentration of typical Mikulich cells and

plasma cells gradually decreases, but hyaline Roussel "bodies" and hyaline degenerated cells appear. Gradually, with the decrease in specific pathomorphologic features, the verification of scleroma becomes more difficult [2, 8, 10, 11].

Figure 10
Rhinoscleroma (Photo by K.P. Derepa, MD, PhD (1966) [11])

The highest informativity of scleroma verification is inherent in immunological methods. Among them, the reaction of complement fixation with a specific scleromatic antigen (J. Bordet – O. Gengou reaction) is recognized as a classic. Its informativity reached 95-98 % [2, 8, 10, 11]. In Eastern Europe, other immunologic reactions were also used, such as agglutination, indirect agglutination, etc. [2, 8, 10, 11]. We studied the informativeness of the reaction of inhibition of leukocyte migration in the capillary, the reaction of lymphocyte blast transformation after incubation with scleromatic antigen, as well as immunobiophysical methods of investigation (immunothermometry, chemiluminescence, triboluminescence). The advantage of immunological tests is their high informativeness, regardless of the stage of the

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disease, the presence of specific scleromatic infiltrates or the bacteria in sufficient concentration. However, with the discontinuation of the specific scleromatic antigen production, the usement of immunodiagnostics has become much more difficult. The high price and economic inexpediency of its production, standardization and licensing compared to the prevalence of scleroma in Ukraine limit further research in this area.

Figure 11

A sharp narrowing of the nasopharyngeal entrance with the "absence" of the tongue due to its dislocation into the nasopharyngeal lumen due to deformation of the soft palate as a result of scarring of infiltrates in a patient with scleroma (endoscopic picture of the oropharynx)

Recently, the journal Neglected Tropical Diseases (PLoS) published information by C. Fevre et al. (2011) that several laboratories of the Pasteur Institute (Paris, France) are successfully developing and implementing polymerase chain reaction (PCR) for the diagnosis of scleroma into clinical practice [30].

There is no doubt that its introduction into clinical practice will significantly clarify the information about the

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prevalence of scleroma, change the structure of hospitalized patients and, due to early appropriate treatment, should facilitate its clinical course. We can also hope for a decrease in the number of patients with newly diagnosed complicated scleroma with an unfavorable course, accompanied by airway stenosis, anatomical deformities, and dysfunction of neighboring organs.

we can predict an increase in the number of primary registered patients with scleroma with minimal clinical manifestations, and further, with the start of early adequate treatment, a decrease in the number of patients with complicated forms of scleroma and its unfavorable course, including those accompanied by airway stenosis, anatomical deformities and dysfunction of neighboring organs.

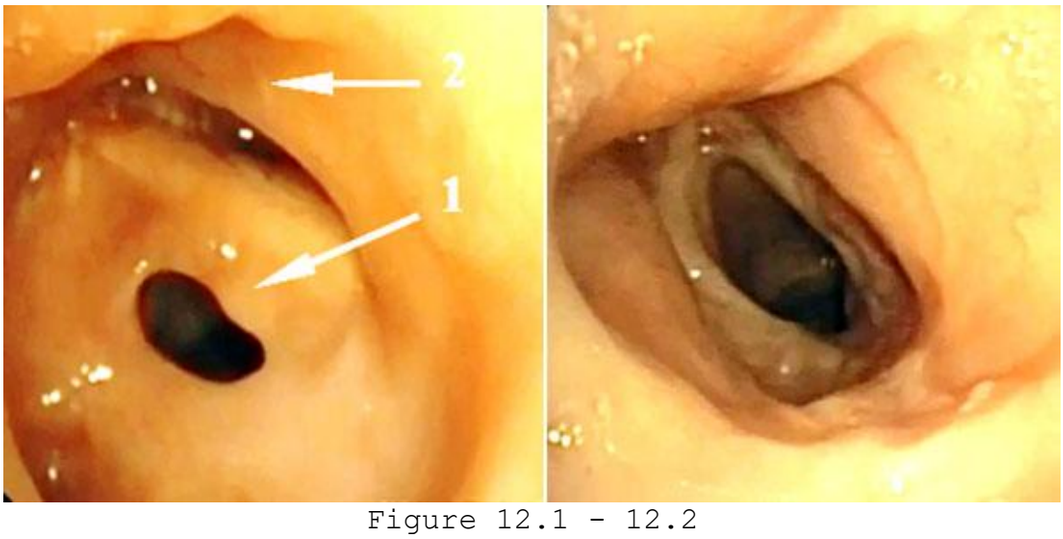

Figure 12.1 - 12.2

Concentric scarring of the larynx at the level of the vocal folds (1) in a patient with scleroma before treatment (2 - vestibular fold) and 5 months after the destruction of the concentric laryngeal narrowing

Conclusions. Thus, the widespread usement of antibacterial substanses in recent decades has reduced the prevalence of scleroma and influenced the features of its clinical course; multiantibioticoresistance of Klebsiella rhinoscleromatis supports the existence of endemic foci of scleroma; with the widespread introduction of polymerase

chain reaction in clinical practice for the verification of scleroma, we can predict an increase in the number of registered patients with scleroma with minimal clinical manifestations, and further, with the start of early adequate treatment, a decrease in the number of patients with complicated forms of scleroma and its unfavorable course, including those accompanied by airway stenosis, anatomical deformities and dysfunction of neighboring organs.

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