The differences of carbohydrate residues distribution in structures of the Schneiderian membrane of different groups was reliable between group of odontogenic maxillary sinusitis and the traumatic form of iatrogenic maxillary sinusitis. The differences of carbohydrate residues between the structures of the Schneiderian membrane was reliable in the group of odontogenic maxillary sinusitis and in the group of medicamentous form of iatrogenic maxillary sinusitis. The differences between saturation of the normal “lamina propria” of Schneiderian membrane and changed with fibrosis are reliable in the group of odontogenic maxillary sinusitis and in the group of medicamentous form of iatrogenic maxillary sinusitis. Distribution of carbohydrate residues differs in different groups of iatrogenic maxillary sinusitis.

**Keywords:** stomatologically maxillary sinusitis, ectin histochemistry of the Schneider membrane.

The work is a part of the research project “Improvement of the bone plastic methods in removing defects and deformations of the face and jaws,” state registration number 0116U004077.

The share of the maxillary sinusitis in the total number of inflammatory diseases of the paranasal sinuses is 56.0 - 73.0 %, and among the purulent - inflammatory processes of the maxillofacial region - up to 21.3 % [5]. According to various epidemiological studies, the incidence of maxillary sinusitis increases annually by 1.5 - 2.0 %. Over the past 10 years, the incidence has tripled [7]. The number of sinusitis associated with stomatological manipulation increased [6]. Our observations show, the presence of a direct relationship between the nature of stomatological manipulations preceding the development of inflammation in the sinus and the picture of the disease. Changes in the body of a local and general nature on the background of stomatological treatment, as well as the presence of concomitant diseases determine the manifestation of a certain type of symptoms of sinusitis and the degree of their severity. With a view to a more detailed study of the features of the formation and course of stomatogenous maxillary sinusitis, we proposed an etio-pathogenetic classification of its various forms [5]. In the frequency and nature of certain clinical, radiologic, morphological and ultrasound symptoms of these forms revealed statistically significant differences.

Since the glycosylation of glycoproteins in the inflammatory focus depends on the type and stage of a particular disease [10] there are fundamentally new approaches to differential diagnosis of diseases, which are based on the detection of glycoprotein. One way to identify the carbohydrate profile of the glycoprotein is the use of carbohydrate-binding proteins - lectins [1].
The purpose of the work was to study the features of the chronic mucositis course in various etiopathogenetic forms of stomatogenic maxillary sinusitis using the method of histochemistry of lectins.

**Material and methods.** Sampling of biomaterial (a portion of the mucous membrane of the maxillary sinus) was performed by in 129 (100.0 %) patients, which were distributed according to etiopathogenetic groups of stomatological maxillary sinusitis [2]. Into the group of odontogenic form (control group) of stomatogenic maxillary sinusitis there were 14 (10.9 %) patients (in the age of 35.3 ± 2.4 in average) who had inflammation in the sinus developed from previously untreated teeth. Into the group of infectious-allergic form of iatrogenic maxillary sinusitis there were 22 (19.1 %) patients (in the age of 40.5 ± 12.7 in average) who had established a periapical infection of previously treated teeth in the sinus in the etiology of the disease; The group of the mixed form of iatrogenic maxillary sinusitis included 24 (20.9 %) patients (in the age 40.2 ± 14.0 in average) with a filling material or a fragment of the tooth root in the clearance of the sinus. 12 (10.4 %) patients (in the age 57.6 ± 4.5 in average) who had the maxillary sinusitis developed in the background of stomatological manipulations and the presence of concomitant chronic diseases accompanied by long reception of hormones, antibiotics or drugs were included in the group of medicamentous (drug) form. In the group of traumatic form of iatrogenic maxillary sinusitis – 57 (49.6 %) patients (in the age 43.8±14.0 in average) with sinusitis that developed against surgical manipulations in the area of the alveolar process or the body of the upper jaw.

The biopsies were fixed in a 10 % neutral formalin solution for 48 hours. Dehydration was carried out in an ascending battery of alcohols, starting with 50.0 % ethyl alcohol, as an intermediate medium, a solution of chloroform was used. Then poured a mixture of paraffin: wax: rubber at a rate of 20: 1: 1. From paraffin blocks on a rotary microtome, 100-150 serial histological sections with a thickness of 5 μm were made. For observational microscopy, histological sections were stained with hematoxylin and eosin. The preparations were processed using the standard sets of "Lectinotest", Lviv in the dilution of lectin 1:50 according to the recommended procedure.

Visualization of binding places of lectin was carried out in the system of dianaminobenzidine - hydrogen peroxide. Control of the specificity of the reaction was carried out by eliminating dianaminobenzidine from the treatment regimen. Specificity of lectins to terminal non-reducing monosaccharide residues of glycoconjugates is given according to literature data: lectin of "golden rain" shrub (LABA), specific for α-L-fucose (αL-Fuc); lectin of soybean (SBA), specific for N-acetyl-D-galactosamine (α-NAcDGal); lectin of wheat germ (WGA), specific for N-acetyleneuraminic acid (NAcDGlc → NAcNeu) and for N-acetylD-galactosamine (α-NAcDGal); lectin of pea (PSA) - to α-D-glucose and α-D-mannose (C6H12O6); lectin of peanut (PNA) specific for βD-galactose (βDGal→R); lectin of black elderberry (SNA) – to sialyl(α2-6) galactose (Neu5Acα2-6Gal); lectin of Concavalin A (Con A) - to D-mannose - R [1]. The abbreviated name of lectins is given in accordance with the international nomenclature of lectins. The intensity of staining of sections with lectins was evaluated by a semi-quantitative method: "+++") - intensive reaction (brown color); "++" - moderate reaction (golden brown color); "+" - weak reaction (golden yellow color); 0 - no reaction, which corresponded to the balles of 3, 2, 1, 0. The use of an ordinal scale for the intensity of staining allowed us to statistically evaluate the differences in the concentrations of glycoproteins in certain structures in the control (odontogenic form stomatogenous maxillary sinusitis) and other studied groups. A nonparametric Mann-Whitney's criterion U to (pu) was used for the ranks of pairwise comparison of the material in the study groups with data in the control group; an analogue of the Kruskel-Wallis criterion (pk-u) was used for a one-parameter and variance analysis - for simultaneous multiple comparison of data from three or more basics groups.

The photodocumentation was carried out using a computerized analysis system consisting of an Axiolab binocular microscope, an Axiocam digital video camera with an 8 megapixel matrix, a video adapter connected to a microscope, a personal computer equipped with a video capture card connected to a digital camera via an interface and a video cable and the software "AxioVision 4.8", allowing you to view the image of the histological preparation on the screen in real time, select the necessary area for the photographs to obtain a digital image of the histological preparation, to save it on the hard disk of the personal computer.

The study was conducted with the participation of DM., prof. Grigorieva EA - Department of human anatomy, operative surgery and topographic anatomy of ZSMU. We thank. prof. Grigorieva Elena for providing the control samples for this study.

**Results of the study and their discussion.** The mucous membrane covering the respiratory system is a biochemically complex medium rich in glycoproteins, antimicrobial peptides, immunoglobulins and many other proteins, lipids and electrolytes. It is divided into an outer loose layer
of proteolytic cleaved mucins, in which the bacteria mainly settle, and an inner layer that is firmly attached to the epithelium, since it is formed by transmembrane glycoproteins [8]. It is suspected that glycoconjugate alterations are correlated with the transformation of chronic maxillary sinusitis with hyperplasia of the sinus mucosa and hypersecretion. The benefit of using the lectin binding method for glycoconjugate analysis is that it specifically identifies the carbohydrate residues in cells and tissues. The carbohydrate moieties of cell surfaces are involved in cell-to-cell interaction and are thought to be important in cell functions, including intercellular recognition and cell maturation [4]. Alteration of the microenvironment and local inflammatory reactions in a variety of diseases may influence cell surface carbohydrate moieties [9].

The normal maxillary sinus epithelium composes of ciliated columnar epithelium in the surface layer and cuboidal epithelial cells in the basal layer, intermingled with goblet cells. The lectin binding pattern of normal epithelium showed that ConA reacted with all epithelial layers, with strong staining in the cilia. WGA showed strong positive staining in the cilia and positive staining in goblet cells and mucous glandular cells of the submucosa. Other lectins, SBA and DBA, don't stain the sinus mucosa except for weak positive staining in the granules of the supranuclear area. Morphological signs of chronic mucositis have been identified in all groups. Expression of β-D-galactose in ciliated cells in groups of traumatic (++), mixed (++), of medicamentous (drug) form (++) and infectious-allergic (+++) form of iatrogenic maxillary sinusitis was higher than in control group (+) (figure 1). In the group of patients with an infectious-allergic form, high expression of β-D-galactose (+++) of sinusitis is noted on the background of more pronounced inflammation symptoms vis-a-vis to other forms.

Accumulation of β-D-galactose in goblet cells of Schneider's membrane of patients in the groups of mixed and medicamentous (drug) forms of iatrogenic sinusitis were minimal (+). It's indicating a lower secretory activity of these cells. The saturation of β-D-galactoses was average (+++) in the remaining groups. The concentration of glycoproteins with terminal residues of β-D-galactose (+) was the same in the basal membrane in traumatic, mixed and of medicamentous (drug) forms of iatrogenic sinusitis; β-D-galactose was completely absent in places (0) in odontogenic sinusitis (control) and infectious-allergic form of iatrogenic sinusitis (pk-u = 0.058).

The concentration of carbohydrate residues of syalic acid (Neu5Aco2-6Gal) in the ciliary cells of the control group (++) was higher than in the group with the traumatic form (pu = 0.66) and the drug form (pu = 0.88) (+); L-fucose (+++) is higher in control than in the infectious-allergic group (+) (pu = 0.5) and of medicamentous (drug) group (+) (pu = 0.88) (pk-u = 0, 73). The saturation of sialic acid (Neu5Aco2-6Gal) in ciliated cells with mixed (+ / ++) and infectious-allergic (++) forms of iatrogenic sinusitis was almost identical (pu = 0.56). The concentration of sialic acids rises in body fluids during inflammatory processes. Binding of proteins with syalic acid determines the negative charge of glycoprotein molecules, sialic acids determine elongated form of their molecules and, as a consequence, high viscosity of these glycoproteins in mucous membranes of the respiratory tract.

This provides protection of mucous membranes from mechanical and chemical damage in time the inflammatory processes.

These changes are used by researchers as an indicator of the activity of the inflammatory process [9]. At present, the attention of scientists around the world has attracted so-called minor sugars: mannose and fucose, which possess prebiotic and immunostimulating properties. Numerous data have been accumulated about their participation in the most important processes of molecular and cellular recognition, the synthesis of hormones and immunoglobulins.

Residues of D-mannose in the study groups were
Outline of the distribution of carbohydrate residues in the structures of the Schneiderian membrane in figure 2. The concentration of carbohydrate residues of sialic acid (Neu5Acα2-6Gal) in the composition of intracytoplasmic inclusions of ciliated cells and cilia of epithelium of the maxillary sinus mucosa in traumatic form (+) was lower than in odontogenic sinusitis (++) (fig. 3). This indicates that mucociliary activity and viability of ciliated epithelium of patients with traumatic form of iatrogenic maxillary sinusitis was lower than in control group. But the accumulation of the benzidine tag in the intracytoplasmic inclusions of basal (+) and goblet (++ / +++ ) cells of patients with traumatic form of iatrogenic sinusitis was more intense than in control group: basal – (0), goblet – (+). The revealed changes can characterize relatively overestimated activity of goblet cells of the maxillary sinuses during inflammation on the background of surgical trauma. This form of iatrogenic sinusitis is accompanied by oroanthral fistula in 98.0% of cases. These patients have the clinical symptoms of inflammation pronounced less in comparison with other study groups. Increasing the secretion of goblet cells can increase the viscosity of mucus, which will slow down the mobility of cilia of the ciliated epithelium, and break the mucozilliare clearance - the protective barrier of the Schneiderian membrane.

The difference in the degree of staining between the structures of the mucous membrane of the maxillary sinuses in the study groups is given in table 1.

Table 1 shows that significant differences between the rates of absorption by various structures of the mucous membrane of the maxillary sinus of the benzidine tag were observed in two etiopathogenetic forms of stomatogental sinusitis: odontogenic sinusitis (control group) (p = 0.0498) and of medicamentous (drug) iatrogenic sinusitis (p = 0.0154). The infectious factor predominates in the pathogenesis of these forms of stomatogental sinusitis. The odontogenic form of the maxillary sinusitis is the youngest of the studied groups and is relatively young: the average age of patients is 35.3 ± 2.4 years. Early development of clinical signs of the disease causes early surgical intervention on the sinuses therefore biopsy sampling could be performed in conditions of pronounced imbalance in the distribution of active glucoproteins. The of medicamentous (drug) form of iatrogenic sinusitis is the oldest - the average age of patients is 57.6 ± 4.5 years, characterized by a long asymptomatic course of the disease on the background of chronic immunodeficiency states. This may cause the disruption and decompensation of the glucoprotein distribution system. In the remaining groups, the difference in the distribution of carbohydrate residues in the structural envelope of the maxillary sinus is less pronounced. This may indicate a positive effect of dental treatment (sanitation) on the course of the maxillary sinusitis.

Signs of the presence of β-D-galactose in the basal cells of the mucosa in odontogenic sinusitis (control group), in traumatic and mixed forms of iatrogenic maxillary sinusitis are noted in a small amount (+). In the group of infectious-allergic form of sinusitis, basal cells contained more (+ / ++) of this carbohydrate residue than in the previous three groups (+), but less than in the group of medicamentous (drug) form iatrogenic sinusitis (++ / +) (pk -u = 0.9). The reason for the relatively high saturation of the deep cell layer with glycoproteins may be the chronic inflammation in the sinus.
(sometimes more than 10 years) of patients with chronic concomitant diseases that cause immunodepression and a lingering asymptomatic sinusitis.

The content of carbohydrate sialic acid residues (Neu5Acα2-6Gal) in the composition of intracytoplasmic inclusions of the epitheliocytes of the mucous membrane of the maxillary sinus in patients with a mixed form of iatrogenic sinusitis is unevenly distributed. In most cases, the cytoplasm of the basal and goblet cells was colored golden color (+), and the cytoplasm of ciliated cells - in golden brown color (+) (pk-u = 0.49). The basal membrane didn't contain SNA + compounds. The fibers of the own plate of the mucosa were also predominantly SNA negative. The saturation of the basal cells of the mucous membrane of the maxillary sinuses in the control group of carbohydrate residues of N-acetyleneuraminic acid (NacDGlс / Neu) was average (++). The color of the cytoplasm of the goblet and ciliary cells was less intense (+) (pk-u = 0.34). The basal membrane was colored light-brown (+) unevenly: areas of the basal membrane were identified, where there were no signs of the presence of receptors for wheats lectin (0). The fibers of the propria of the mucous membrane turned out to be predominantly WGA-negative, except for the lesions of fibrosis (table 2).

Table 2 shows that differences in saturation with carbohydrate residues in normal and fibro-altered fibers of the Schneiderian membrane are significant in traumatic and drug-induced forms of iatrogenic sinusitis. As you can see, the depth of fibrotic changes in odontogenic sinusitis is not expressed. In traumatic sinusitis, postoperative sinusitis is accompanied by severe mucosal fibrosis. Sluggish chronic sinusitis with a medicamentous form leads to fibrosis too.

In patients with traumatic, mixed and infectious-allergic forms of the iatrogenic group of stomatological sinusitis, the concentration of carbohydrate residues of N-acetyl-D-galactosamine (α-NacDGal) was found to be lower (pu = 0.02), which may indicate a reduction of metabolic processes in the mucosa (figure 4).

The basal membrane and the fibers of the mucosa propria in these groups practically didn't contain N-acetyl-D-galactosamine, except for area of fibrosis where the fibers were tan golden brown color (+). Carbohydrate residues of N-acetyleneuraminic acid (NacDGlс / Neu) were most intensively distributed in the composition of necrotic epithelium conglomerates (+++) and in the intracytoplasmic granules of the basal cells of the epithelium of the maxillary sinus mucosa in patients with medicamentous (drug) form of iatrogenic sinusitis. The coloration of the basal membrane, fibers and walls of the vessels of the intrinsic plate was intensive (+++) exclusively in the tissue fibrosis fibers (pu = 0.04). The results of statistical calculations of the reliability of differences in the intensity of saturation with benzidine dye of all structures of the mucous membrane of the maxillary sinuses of patients between the groups under study are given in table 3.

### Table 2

<table>
<thead>
<tr>
<th>Type of Sinusitis</th>
<th>U</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Control (control)</td>
<td>1.00</td>
<td>0.053009</td>
</tr>
<tr>
<td>Traumatic form of iatrogenic maxillary sinusitis*</td>
<td>0.00</td>
<td>0.019360*</td>
</tr>
<tr>
<td>Mixed form of iatrogenic maxillary sinusitis</td>
<td>7.00</td>
<td>0.880933</td>
</tr>
<tr>
<td>Infectious-allergic form of iatrogenic maxillary sinusitis</td>
<td>3.00</td>
<td>0.169203</td>
</tr>
<tr>
<td>Medicamentous (drug) form of iatrogenic maxillary sinusitis *</td>
<td>1.00</td>
<td>0.048533*</td>
</tr>
</tbody>
</table>

Note. * - the difference in the figures is reliable

### Table 3

<table>
<thead>
<tr>
<th>Type of Sinusitis</th>
<th>Kraskel-Wallis Criterion Value: H</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Control (control)</td>
<td>3.69</td>
<td>0.59</td>
</tr>
<tr>
<td>Traumatic form of iatrogenic maxillary sinusitis*</td>
<td>13.94</td>
<td>0.016*</td>
</tr>
<tr>
<td>Mixed form of iatrogenic maxillary sinusitis</td>
<td>7.5</td>
<td>0.19</td>
</tr>
<tr>
<td>Infectious-allergic form of iatrogenic maxillary sinusitis</td>
<td>5.14</td>
<td>0.39</td>
</tr>
<tr>
<td>Medicamentous (drug) form of iatrogenic maxillary sinusitis</td>
<td>3.30</td>
<td>0.65</td>
</tr>
</tbody>
</table>

Note. * - the difference in the figures is reliable
As can be seen from Table 3, differences in the expression of carbohydrate residues with the control group were significant in the group with traumatic iatrogenic maxillary sinusitis (p = 0.016). In groups where the prevailing factor of the pathogenesis of the disease was infection, and not trauma, the differences are not reliable. The presence of α-L-fucose (Fucα1-2Gaβ1-4Glc) was intense (++++) in ciliated cells of the maxillary sinus mucosa of patients with traumatic, mixed forms of iatrogenic sinusitis and in the control group. Expression of α-L-fucose in infectious-allergic group and medicamentous (drug) forms was weak (+). The α-L-fucose was equally saturated (+ / ++) in the basal membrane of patients with odontogenic sinusitis (control), with traumatic and infectious-allergic groups of iatrogenic sinusitis. This was exceeded the content of carbohydrate residue in the groups of mixed and drug iatrogenic sinusitis (+), α-L-fucose was above (++), as part of intra-cytoplasmic inclusions of basal cells of traumatic and drug forms, and in goblet cells and in mixed form than in control (+), indicating a change in the properties of secretion and mucus as a whole, (pk-u = 0.49).

**Conclusions**

1. The difference in the intensity of the distribution of carbohydrate residues in the traumatic and medicamentous iatrogenic maxillary sinusitis groups with the one-genic form of the maxillary sinusitis was significant.

2. The differences between saturation of the normal “lamina propria” of Schneiderian membrane and changed with fibrosis are reliable in the group of odontogenic maxillary sinusitis and in the group of medicamentous form of iatrogenic maxillary sinusitis

3. Distribution of carbohydrate residues differs in different groups of iatrogenic maxillary sinusitis. Differences between the groups in the basis of the etiology of which there is an infectious factor aren’t reliable.

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 yatrogенного розподілу вуглеводних синусит етиології недостатності (УДК 616.36-06:616.61-008.64:616.149-008.341.1

УДК 616.36-06:616.61-008.64:616.149-008.341.1

ГІПОСІЯ-ІНДУЦІБЕЛЬНИЙ ФАКТОР ЯК МОЛЕКУЛЯРНА МІШЕНЬ ПРИ ГЕПАТОРЕНАЛЬНОМУ СИНДРОМІ

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Гепатorenальний синдром (ГРС) є серйозним ускладненням алкогольного цирозу печінки (АЦП). Вибачення механізмів молекулярної відповіді на гіпокію при ГРС є перспективним напрямком досліджень у гепатології. Метою роботи була оцінка ролі гіпосія-індуцібельного фактору HIF-1α в патогенезі ГРС у умовах гострої-на-хронічної (ГХПН) печінкової недостатності (ХПН) у пацієнтів із АЦП, 150 пацієнтів з АЦП+ГРС були поділені на 2 групи: I група (n=67) – ХПН, II група (n=83) – ОХПН. Показник рівня HIF-1α у найважчій категорії хворих групи 2, з IV стадією за шкалою CLIF-C-ACLF, майже в три рази перевищував такий у аналогічній категорії з групи 1, з класом С по Чайлд-Пью, і становив 30±7,9 pg/ml. Різке підвищення рівня HIF-1α у 2-й групі з IV стадією за шкалою CLIF-C-ACLF засвідчуює важливість вивчення гіпосії, що обумовлена значним погіршенням спаечнів молекулярної кровопливлі і спазмом ниркових судин при ГРС. Рівень HIF-1α тісно корелює із показниками печінково-ниркової недостатності у обстежених хворих з АЦП+ГРС, що дозволяє використовувати його як індикатор у комплексній діагностиці даного захворювання.

Ключові слова: гепатorenальний синдром (ГРС), алкогольний цироз печінки (АЦП), гіпосія-індуцібельний фактор, печінково-ниркова недостатність

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Ключові слова: гепатorenальний синдром (ГРС), алкогольний цироз печінки (АЦП), гіпосія-індуцібельний фактор, печінково-ниркова недостатність

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