

# Immunological Aspects of Diagnosis and Treatment of Sick Children with Chronic Purulent Medium Otititis on the Background of Chronic Hepatitis B

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**Abstract** The immunograms of 93 sick children with chronic purulent otitis media on the background of chronic hepatitis (39 mesotympanitis and 54 epitympanitis) were studied. A comparative analysis of immunogram indices was carried out depending on the severity of inflammatory changes and the inclusion of imunofan in the therapy regimen. The results of the work showed that in sick children with chronic purulent otitis media against the background of chronic hepatitis, the immunogram reflects the peculiarities of the course of the inflammatory process. Chronic inflammatory process in the temporal bone and surgical trauma sharply suppress cellular and humoral immunity, which prompts the use of immunocorrectors in the scheme of postoperative treatment. The inclusion of imunofan in the therapy scheme allowed to completely normalize the immunogram indices in patients with epitympanitis and to improve the clinical course of the postoperative period.

**Keywords** Chronic hepatitis, Immunogram, Cellular and humoral immunity, Imunofan, Chronic otitis media

## 1. Introduction

The modern literature provides a lot of data on the relationship between the development of a viral infection and pronounced changes in the immune system, which are classified as secondary immunodeficiency states [5,6,12]. An increase in the number of chronic inflammatory diseases of the middle ear against the background of chronic hepatitis and a change in their clinical course [1,9,13] dictates the need for an in-depth study of the mechanisms of development of this pathology and the development of pathogenetic effects on the chronic inflammatory process. It is known that one of the reasons for the formation of chronic purulent otitis media on the background of chronic hepatitis is a change in general and local immunity [3,7,14]. The main indicators of cellular and humoral immunity are combined by the concept of "immunogram" [4,5,10,11]. Imunofan is used to correct immunological disorders as part of the combination therapy of a number of diseases [2,8,15]. However, information about the use of imunofan in otorhinolaryngology, including in the treatment of epitympanitis, is not found in the literature. Objective: to study the immunogram parameters in patients with chronic purulent otitis media and to evaluate the effectiveness of standard and combined therapy with the use of imunofan.

## 2. Materials and Methods

On the first day of hospitalization, the immunograms of 93 patients with chronic purulent otitis media (51 boys, 42 girls) were examined. All examined patients, depending on the activity of the inflammatory process, were divided into three groups. The first group consisted of 27 patients with mesotympanitis (code H66.1 according to the International Classification of Diseases) who received only conservative therapy. The second group consisted of 28 patients with epitympanitis (code 66.2), who simultaneously underwent sanitizing and functional operations on the middle ear. The third group included 38 patients with epitympanitis who, due to the vastness of pathological changes (a significant amount of destructive destruction, large cholesteatoma, labyrinth fistula, sub- and epidural abscesses, facial nerve paresis), underwent only a sanitizing operation.

Upon discharge from the hospital, the immunogram was analyzed in 54 patients with epitympanitis, of which two groups were formed. The control group included 26 patients who underwent standard therapy in the postoperative period (antibiotics, hyposensitizing drugs, symptomatic and local therapy), the main group consisted of 28 patients who, upon discharge from the hospital, had an immunogram analyzed in 54 patients with epitympanitis, of which two groups were formed. The control group included 26 patients who received standard therapy in the postoperative period (antibiotics, hyposensitizing drugs, symptomatic and local therapy),

the main group consisted of 28 patients who received standard postoperative treatment enhanced by intramuscular administration of imunofan 1 ml every other day for 10 days (5 injections). The material was processed using a set of descriptive statistics parameters implemented in the Microsoft Excel analysis package for Windows XP. The differences in relative and absolute values were determined using the critical values of the Student's criterion (t). The differences at  $t > T$  critical were considered reliable, corresponding to the significance level  $p < 0.05$ .

The results of the study of immunograms of patients with chronic purulent otitis media indicated significant changes in the key links of both cellular and humoral immunity. In clinical groups, there is an increasing suppression of all links of immunity with an increase in the severity of the inflammatory process (Table 1). In the cellular immunity of patients of the first clinical group, although there is a decrease in the number and functional activity of phagocytes, significant differences in indicators are determined only by the number

of active phagocytes -  $1.7 \pm 0.17 \times 10^9 / l$  ( $p < 0.05$  to the indicators of healthy donors). In patients of the second group, the inhibition of cellular immunity increases, the percentage of phagocytosis decreases to  $49.4 \pm 2.9\%$  ( $p < 0.05$ ), the phagocytic number to  $4,610,31$  ( $p < 0.05$ ), the number of active phagocytes - up to  $1.3 \pm 0.12 \times 10^9 / l$  ( $p < 0.05$ ). In the third clinical group, the percentage of phagocytosis and the number of active phagocytes in none of the patients reached the lower limit of the reference interval, and the average figures were significantly lower than the average values of similar indicators in the first and second groups. The percentage of phagocytosis in the third group decreased to  $38.9 \pm 3.6\%$  ( $p < 0.05$ ), the phagocytic number - to  $4.1 \pm 0.45$  ( $p < 0.01$ ), the number of active phagocytes - to  $1.51 \pm 0.19 \times 10^9$  ( $p < 0.01$ ) (Table 1). The deepest depletion of the cellular link of immunity was found in patients with a long-term destructive cholesteatoma process in the temporal bone and a relapse of epitympanitis after a previously performed sanitizing operation.

**Table 1.** Average immunogram values in patients with chronic purulent otitis media, depending on the severity of the inflammatory process

Indicator	Healthy donors	Group 1 n = 27	Group 2 n = 28	Group 3 n = 38
Leukocytes, $\times 10^9/l$	<b><math>5,4 \pm 0,1</math></b>	<b><math>5,4 \pm 0,23</math></b>	<b><math>5,8 \pm 0,24</math></b>	<b><math>6,2 \pm 0,37</math></b>
Lymphocytes, $\times 10^9/l$	<b><math>1,7 \pm 0,01</math></b>	<b><math>1,6 \pm 0,12</math></b>	<b><math>1,6 \pm 0,11</math></b>	<b><math>1,8 \pm 0,05</math></b>
Relative T-lymphocytes, %	<b><math>53,9 \pm 0,3</math></b>	<b><math>54,8 \pm 5,6</math></b>	<b><math>68,1 \pm 3,9T</math></b>	<b><math>47,2 \pm 3,1</math></b>
absolute T-lymphocytes, $\times 10^9/l$	<b><math>0,95 \pm 0,04</math></b>	<b><math>1,4 \pm 0,22</math></b>	<b><math>1,8 \pm 0,211</math></b>	<b><math>1,3 \pm 0,17</math></b>
B-lymphocytes are relative, %	<b><math>14,7 \pm 0,3</math></b>	<b><math>22,9 \pm 0,9</math></b>	<b><math>22,5 \pm 0,8</math></b>	<b><math>15,8 \pm 0,7</math></b>
B-lymphocytes are absolute, $\times 10^9/l$	<b><math>0,4 \pm 0,01</math></b>	<b><math>0,53 \pm 0,7f</math></b>	<b><math>0,55 \pm 0,6T</math></b>	<b><math>0,42 \pm 0,5</math></b>
Percentage of phagocytosis, %	<b><math>82,8 \pm 0,2</math></b>	<b><math>59,3 \pm 2,51</math></b>	<b><math>49,4 \pm 2,91</math></b>	<b><math>38,9 \pm 3,6</math></b>
Phagocytic number	<b><math>7,1 \pm 0,1</math></b>	<b><math>6,9 \pm 0,26</math></b>	<b><math>4,6 \pm 0,31</math></b>	<b><math>4,1 \pm 0,45</math></b>
Number of active phagocytes, $\times 10^9/l$	<b><math>2,7 \pm 0,1</math></b>	<b><math>1,7 \pm 0,17</math></b>	<b><math>1,3 \pm 0,12</math></b>	<b><math>1,5 \pm 0,19</math></b>
Circulating immune complexes, ED	<b><math>53,8 \pm 0,2</math></b>	<b><math>31,2 \pm 5,5</math></b>	<b><math>30,7 \pm 5,7</math></b>	<b><math>21,2 \pm 4,1</math></b>
Immunoglobulin G, g/l	<b><math>9,06 \pm 0,1</math></b>	<b><math>11,2 \pm 0,4</math></b>	<b><math>10,7 \pm 0,4</math></b>	<b><math>11,4 \pm 0,4</math></b>
Immunoglobulin A, g/l	<b><math>1,25 \pm 0,1</math></b>	<b><math>1,48 \pm 0,1</math></b>	<b><math>1,39 \pm 0,1</math></b>	<b><math>1,27 \pm 0,1</math></b>
Immunoglobulin M, g/l	<b><math>1,14 \pm 0,1</math></b>	<b><math>0,6 \pm 0,04.1</math></b>	<b><math>0,7 \pm 0,05</math></b>	<b><math>0,8 \pm 0,06</math></b>

Note. Significant differences with indicators in healthy individuals ( $p < 0.05$ ) are highlighted in bold, arrows indicate indicators that go beyond the reference interval.

**Table 2.** Average immunogram values in patients with epitympanitis before discharge from the hospital, depending on the use of Immunophane

Indicator	Healthy donors	Standard therapy n = 26	Imunofan n = 28
Leukocytes, $\times 10^9/l$	<b><math>5,4 \pm 0,1</math></b>	<b><math>5,7 \pm 0,17</math></b>	<b><math>5,5 \pm 0,22</math></b>
Lymphocytes, $\times 10^9/l$	<b><math>1,7 \pm 0,01</math></b>	<b><math>1,69 \pm 0,08</math></b>	<b><math>1,71 \pm 0,11</math></b>
Relative T-lymphocytes, %	<b><math>53,9 \pm 0,3</math></b>	<b><math>58,8 \pm 4,4</math></b>	<b><math>69,1 \pm 5,9T</math></b>
absolute T-lymphocytes, $\times 10^9/l$	<b><math>0,95 \pm 0,04</math></b>	<b><math>1,6 \pm 0,19 j</math></b>	<b><math>1,4 \pm 0,13</math></b>
B-lymphocytes are relative, %	<b><math>14,7 \pm 0,3</math></b>	<b><math>21,5 \pm 0,19f</math></b>	<b><math>16,2 \pm 0,26</math></b>
B-lymphocytes are absolute, $\times 10^9/l$	<b><math>0,4 \pm 0,01</math></b>	<b><math>0,53 \pm 0,04f</math></b>	<b><math>0,47 \pm 0,05</math></b>
Percentage of phagocytosis, %	<b><math>82,8 \pm 0,2</math></b>	<b><math>29,4 \pm 3,11</math></b>	<b><math>71,3 \pm 4,4</math></b>
Phagocytic number	<b><math>7,1 \pm 0,1</math></b>	<b><math>3,6 \pm 0,41</math></b>	<b><math>8,7 \pm 0,62</math></b>
Number of active phagocytes, $\times 10^9/l$	<b><math>2,7 \pm 0,1</math></b>	<b><math>1,2 \pm 0,1 J</math></b>	<b><math>2,6 \pm 0,19</math></b>
Circulating immune complexes, ED	<b><math>53,8 \pm 0,2</math></b>	<b><math>22,4 \pm 4,9</math></b>	<b><math>51,9 \pm 5,21</math></b>
Immunoglobulin G, g/l	<b><math>9,06 \pm 0,1</math></b>	<b><math>8,9 \pm 0,58</math></b>	<b><math>13,1 \pm 0,63</math></b>
Immunoglobulin A	<b><math>1,25 \pm 0,1</math></b>	<b><math>1,31 \pm 0,13</math></b>	<b><math>1,45 \pm 0,09</math></b>
Immunoglobulin M	<b><math>1,14 \pm 0,1</math></b>	<b><math>0,66 \pm 0,04</math></b>	<b><math>1,03 \pm 0,06</math></b>

Note: Significant differences with indicators in healthy individuals are highlighted in bold ( $p < 0.05$ ), arrows indicate indicators that go beyond the reference interval.

The average numbers of leukocytes in all clinical groups were recorded within the acceptable reference interval, increasing from the first group to the third, reaching significant differences in the latter with indicators in healthy donors -  $6.2 \pm 0.37 \times 10^9/l$  ( $p < 0.05$ ). In patients of the first and second groups, the intensity of humoral immunity was noted, expressed in an increase in the number of T- and B-lymphocytes, especially noticeable in young patients. In the third group, there was no adequate immunological response to the chronic process. Despite the predominance of patients with pronounced inflammatory changes in the temporal bone, including recurrent and complicated, the absolute and relative numbers of T- and B-lymphocytes were within acceptable reference numbers (Table 1).

The increasing immunosuppression is also seen by other indicators of humoral immunity. In all clinical groups, both in general and throughout the sample, there is a decrease in the titer of circulating immune complexes. In the first group, their figures were  $3 \pm 5.5$  units, in the second they decreased to  $30.7 \pm 5.7$  units, in the third - to  $21.2 \pm 4.1$  units. Similarly, immunoglobulin A titers decreased: from  $1.48 \pm 0.1$  g/l in the first group, to  $1.39 \pm 0.1$  g/l in the second and  $1.27 \pm 0.1$  g/l in the third (Table 1).

The results of comparing the indicators of cellular and humoral immunity in clinical ipynx revealed an increasing immunodeficiency in patients with chronic purulent otitis media, depending on the severity of inflammatory changes. This circumstance encourages the inclusion in the treatment regimen, especially severe destructive cholesteatoma, recurrent and complicated epitympanitis, immunocorrecting drugs.

Analysis of the results of the immunogram before discharge showed significant changes in the cellular and humoral immunity in patients with chronic purulent otitis media after sanitizing surgical treatment. Such a condition after surgical treatment is described by many authors as "immunological paralysis". Thus, a sharp decrease in phagocytic activity was noted in patients of the control group. The percentage of phagocytosis in them was  $29.4 \pm 3.1\%$  ( $p < 0.05$  to the indicators of healthy donors), the phagocytic number was  $3.6 \pm 0.41$ , the number of active phagocytes was  $1.2 \pm 0.1 \times 10^9/l$  (reference interval  $2.5 - 2.9 \times 10^9/l$ ,  $p < 0.05$ ) (Table 2). The data obtained confirm the fact of the immunosuppressive effect of surgical trauma and indicate the low immunocorrective effectiveness of traditional therapy prescribed in the postoperative period.

It was noted that in most patients who received only 29.4 standard therapy, absolute and relative numbers of T- and B-lymphocytes were higher than in healthy donors, which affected the average indicators. Relative T-lymphocytes were  $58.8 \pm 4.4\%$ , absolute -  $1.6 \pm 0.19 \times 10^9/L$ , B-lymphocytes -  $21.5 \pm 0.19\%$  and  $0.53 \pm 0.04 \times 10^9 /l$ . At the same time, a sharp decrease in the functional activity of cells was noted. Low indicators of circulating immune complexes were noted -  $22.4 \pm 4.9$  units ( $p < 0.05$  to the indicators of healthy donors), immunoglobulin G -  $8.9 \pm 0.58$  g/l, immunoglobulin A -  $1.21 \pm 0.13$  g/l and immunoglobulin M -  $0.66 \pm 0.04$  g/l (Table 2).

The inclusion of immunofan in the scheme of postoperative treatment of patients with chronic purulent otitis media allowed to normalize most indicators of cellular and humoral immunity by the time of discharge from the hospital. The percentage of phagocytosis in this group of patients was  $71.3 \pm 4.4\%$  ( $p < 0.05$  to control), the phagocytic number was  $8.7 \pm 0.62$  ( $p < 0.05$  to control), the number of active phagocytes was  $2.6 \pm 0.19 \times 10^9/l$  ( $p < 0.05$  to control). The absolute and relative numbers of T- and B-lymphocytes, although determined at the level of the maximum figures of the reference interval, did not significantly differ from those in patients who received standard therapy (Table 2).

The use of immunofan activated the functional activity of immunocytes. On average, all the compiled documents of humoral immunity are determined at the level of the highest granites of the reference interval and are significant from the indications in large ones treated according to the traditional scheme ( $p < 0.05$ ). Thus, the average levels of circulating immune complexes increased to  $51.9 \pm 5.21$ , immunoglobulin G - to  $13.1 \pm 0.63$  g/l, immunoglobulin A - to  $1.55 \pm 0.09$  g/l, immunoglobulin M - to  $1.03 \pm 0.06$  g/l (Table 2).

Combined immunofan therapy of postoperative patients with epitympanitis significantly reduced the percentage of patients with a high degree of immunological insufficiency. By the time of discharge from the hospital in 82.6% of patients who received only standard therapy, at least 5 immunogram indicators exceeded the limits of the reference interval. The administration of immunofan allowed to reduce the proportion of patients with such immunological disorders to 14.8% ( $p < 0.05$ ).

The beneficial effect of using immunofan in the postoperative period in patients with epitympanitis is noticeable not only in the restoration of immunological, but also in positive changes in the clinical status of patients. In most patients, by the time they were discharged from the hospital (8-12 days), exudation from the postoperative cavity was scanty, areas of epidermization began to appear.

Thus, in patients with chronic purulent otitis media, the immunogram reflects the features of the course of the inflammatory process, which must be taken into account in the diagnosis and treatment regimen. Chronic inflammatory process in the temporal bone and surgical trauma sharply inhibits cellular and humoral immunity, which prompts the use of immunocorrectors in the scheme after surgical treatment. The inclusion of Immunophane in the therapy regimen made it possible to completely normalize the immunogram indicators in children with epitympanitis and improve the clinical course of the postoperative period.

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