



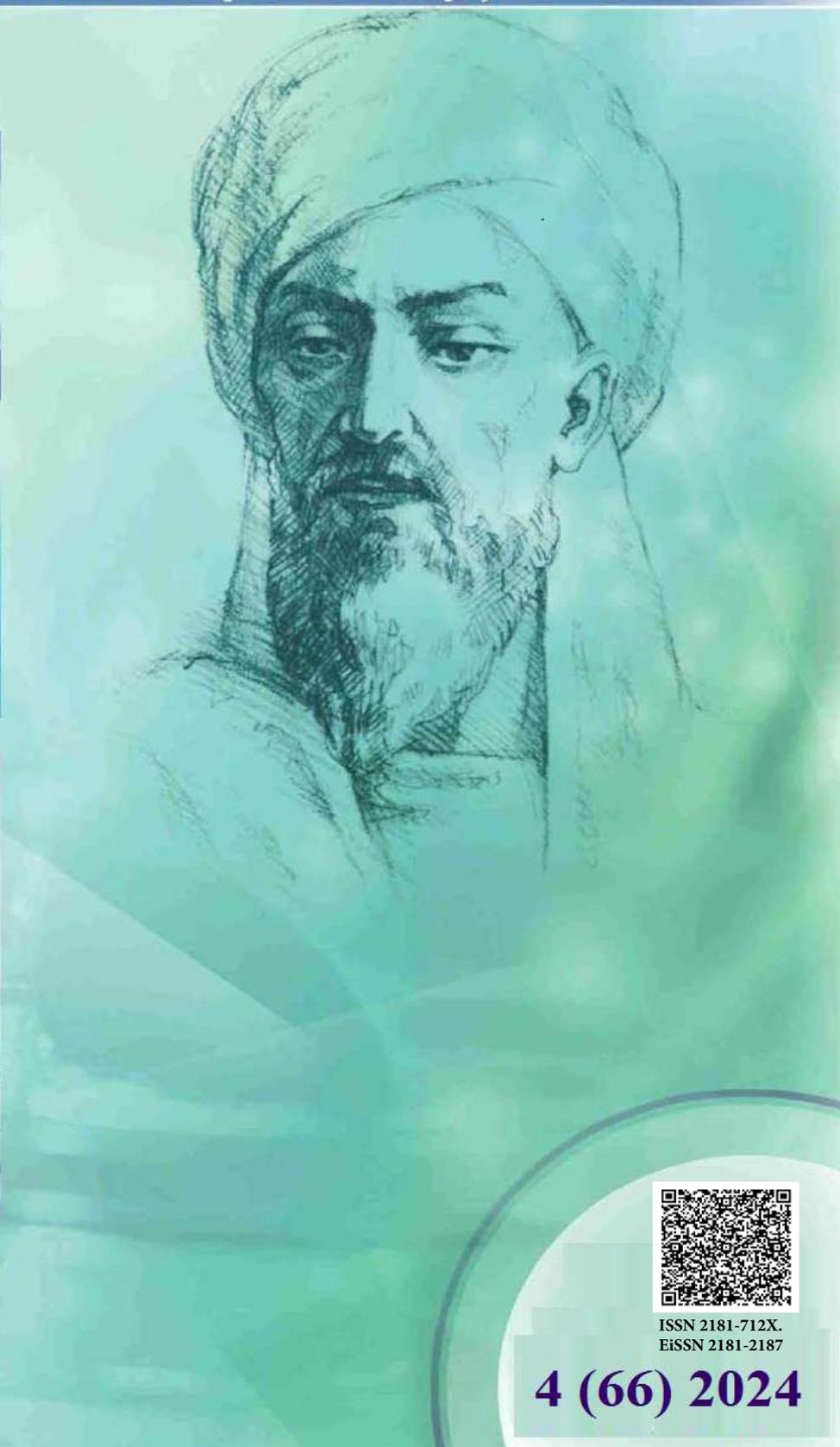
**New Day in Medicine**  
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## ALGORITHM FOR DIAGNOSIS AND TREATMENT OF METAPHYSEAL FORMS OF ACUTE HAEMATOGENOUS OSTEOMYELITIS OF LONG BONES IN CHILDREN

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### ✓ *Resume*

*The use of the proposed algorithm for diagnosis and surgical treatment made it possible to reduce the complicated course of AChO in the form of transition to a chronic form by 8.3% ( $p = 0.048$ ), and the number of “chronicles” among patients with metaphyseal localization of the process was reduced to zero. We consider MRI, especially in children with metaphyseal localization of the pathological process, and MBI of a bone fragment to be the most effective methods for early diagnosis of AGO of long bones. X-ray, SCT, ultrasound of the extremities and Waldman's test are of little significance and are ineffective in the early period of the disease.*

*Key words: Algorithm for diagnosis and treatment of metaphyseal forms of acute hematogenous osteomyelitis, osteomyelitis of long bones, children*

### Relevance

Acute hematogenous osteomyelitis (AHO) is a severe purulent - septic disease, which is accompanied by various complications, transition to chronic forms, as well as the development of orthopedic pathology and septic condition with frequent lethal outcomes [1, 2]. Due to improved diagnosis and treatment, septic complications and mortality in patients with AHO decreased to 0.5-2.7% [3, 4]. However, the transition to the chronic form remains significant and ranges from 5 to 40% according to various authors [5, 6, 7, 8]. The main reason for the complicated course of acute hematogenous osteomyelitis is a violation of the early diagnosis algorithm, which makes it difficult to provide timely, adequate specialized care [9, 10]. Today, the most substantiated methods for diagnosing and treating AHO (the so-called “gold (criterion) standard”) are the isolation of microorganisms that cause the disease and the widespread use of MRI, including contrast [8, 11]. However, early research data are used in only 4% of observations [12]. Optimal algorithms are also not always used in the treatment of hematogenous osteomyelitis in the acute phase, which leads to worsening the disease and the development of complications, including its chronicity [10-12]. Therefore, the development of an optimal diagnostic algorithm and treatment of acute hematogenous osteomyelitis in children is relevant and timely.

**Aim.** The purpose of the study is to find an optimal algorithm for early diagnosis and treatment of acute hematogenous osteomyelitis of long bones in children to prevent a complicated protracted course of the disease.

**Materials and methods.** In the surgery department of the regional children's clinical hospital, which is the clinical basis of the Department of Pediatric Surgery and Orthopedics of the Rostov Medical University, from 2014 to 2023, 167 children with acute hematogenous osteomyelitis of long bones aged from 3 to 16 years were treated. By gender, boys predominated in the proportion of 2:1. Patients were admitted in the first three days from the onset of the first symptoms of the disease 127 (76%). The remaining 40 patients were admitted to our clinic at various times from 4 to 10 days from the onset of the disease. The criterion of late presentation clearly, according to most authors [1, 2, 4, 8-10], has a positive effect on the chronicity of osteomyelitis of long bones. Therefore, these children were not included in the observation group. Thus, we analyzed the modern possibilities of early diagnosis and optimal treatment of acute hematogenous osteomyelitis of long bones in a regional specialized clinical institution in 127 patients aged 3 to 16 years.

We divided all patients into 2 groups according to the period of treatment at the clinic: the first (control) group included children admitted to the clinic from 2014 to 2018 (67 children), and the second (main) group – from 2019 to 2023 (60 patients) (Table 1).

The pathological focus in most cases was found in the long bones of the lower extremities: in the femur in 53 (41.7%) patients, in the tibia – in 37 (29.2%) children, in the fibula – in 5 (3.9%) children. Osteomyelitis was diagnosed in the long bones of the upper extremities in 32 cases: the humerus in 20 (15.7%) children and the ulna and radius in 12 (9.5%) patients. The localization of the pathological focus in the bone in our study did not have a fundamental effect on the course of the disease.

The diagnosis of AHO is based on an algorithm that includes complaints, anamnestic data, reliable clinical parameters, as well as the results of X-ray, laboratory, and instrumental examination (Table 1).

Clinical examination was performed on all patients. The most significant for diagnosis are complaints of pain in the limb of varying intensity, clinical symptoms in the form of limited function of the limb and painful contracture of the joints, pain with axial load on the limb and when tapping on the bone. Half of the patients suffered from general condition and had a feverish temperature.

**Table 1**

**Absolute and relative indicators of the studied groups (n), (%)**

Patient groups with AHO	Control group (n=67)	Main group (n=60)	p
Methods examinations	67 (100%)	60 (100%)	1,0
X-ray of bones	67 (100%)	60 (100%)	1,0
Laboratory examination	67 (100%)	60 (100%)	1,0
Bacterial blood culture for sterility	38 (56,7%)	35 (58,3%)	0,85
Ultrasound of the limb	21 (31,3%)	44 (73,3%)	<0,0001
SCT of the limb	26 (38,8 %)	17 (28,3%)	0,215
MRI of the limb	—	33 (55 %)	<0,0001
Measuring intraosseous pressure	21 (31,3%)	—	<0,0001
Bacterial culture of intraosseous contents	67 (100%)	60 (100%)	1,0
Microbiological examination of a bone fragment	—	60 (100%)	<0,0001

Note: control group – patients admitted in the period 2014–2018; main group – patients admitted in the period 2019–2023; n – number of patients; % of application of examination methods in the group. The level of significance of differences was assessed using Pearson's Chi square ( $\chi^2$ ) test.

Despite the fact that reliable radiological signs of AHO of long bones appear in the 3rd week from the onset of the disease, we agree with the opinion of V.A. Tarakanov et al. [10] about the need to conduct an X-ray of the affected limb at the patient's first visit to exclude fractures, bone tumors, tuberculous osteitis, etc. In connection with this situation, all patients without exception with suspected AHO underwent radiography of the affected bone according to the standard method in 2 projections.

Laboratory diagnostics were performed in all patients upon admission to the clinic and for monitoring over time. The scope of the examination included a general blood test, CRP, total protein and protein fractions, as well as some other general clinical studies. Bacterial blood culture for sterility was performed in 2/3 of patients in both groups (Table 1).

Ultrasound of soft tissues and joints of the affected limb using the Doppler effect was performed with a linear sensor in the first hours of admission of the sick child. 21 studies were conducted in the

control group, 44 in the main group, which corresponds to 31.3% and 73.3% (2,5 times more in the main group,  $p < 0,0001$ ).

MRI of the limb was not performed in the first group, but in the second group – in 33 children (more than half of those admitted during this period,  $p < 0,0001$ ). SCT of the affected limb segment was performed in only 43 cases, with 26 (38.8%) children in the control group and 17 (28.3%) in the study group ( $p = 0,215$ ).

Surgical interventions were performed in all 127 patients. The scope of surgery for acute osteoporosis included osteoperforation of the affected bone segment in all cases. In patients of both groups, bacterial culture of intraosseous contents and determination of microflora sensitivity to antibiotics were performed.

In addition, intraosseous pressure was measured in one third of the children in the first group. All patients admitted to the clinic in the period 2019–2023. Additionally, microbiological examination of a bone fragment from the affected limb segment was performed.

All patients received broad-spectrum osteotropic antibiotics during the first hours of hospitalization. After receiving the results of bacterial studies, antibacterial therapy was carried out individually according to the sensitivity of the microflora to the drugs.

Studies in groups of patients were conducted in accordance with the ethical standards of the Declaration of Helsinki of the World Medical Association “Ethical principles for conducting scientific medical research involving human subjects” as amended in 2013 and the “Rules of clinical practice in the Russian Federation”, approved by order of the Ministry of Health of the Russian Federation dated June 19, 2003 N 266 and approved by the local independent ethical committee of the Rostov State Medical University of the Russian Ministry of Health. All patients’ parents of all patients who were hospitalized at the clinical hospital signed consent to participate in clinical studies organized on its basis.

Statistical analysis was carried out using the Statistica 12.0 program (StatSoft, USA). We used the frequency analysis module. The difference in proportions in the two groups was compared using the Pearson Chi square ( $\chi^2$ ) test by constructing  $2 \times 2$  contingency tables.

### **Results and discussion**

In patients in the control group, the transition to the chronic form of the disease was noted in 14 (20.9%) children, and in the main group – in 5 (8,3%) ( $p = 0,048$ ).

Most often, the transition of AHO to the chronic form was observed in patients with localization of the pathological focus in the metaphyseal part of the bone. In the control group, a complicated course of hematogenous osteomyelitis was observed in 14 children. In 10 of them, the primary focus was determined in the metaphyseal zone of the long bone, which corresponds to 71% of all patients with a protracted course of the disease. In patients in this group, the diagnosis was made on the basis of a clinical examination, the presence of pathological abnormalities in a general blood test: an increase in the total number of leukocytes, changes in the blood count and an increase in ESR. In addition, we consider an increase in CRP to be more than 10  $\mu\text{g/L}$  as an important criterion in favor of osteomyelitis. Radiography of the long bones revealed no pathologies.

SCT of bones also causes skepticism. At the initial stage of development of acute hematogenous osteomyelitis (intramedullary phase of inflammation), we did not find any significant changes, despite positive assessments of the information content of the method from other authors [9]. When performing ultrasound examination of the affected segments of long bones, pathological changes in the metaphyseal zone of the bone during the first 3 days of the disease were found in only 4 (19%) patients out of 21. The authors observed blurred bone segments, thickening of the periosteum of the metaphysis, and increased vascularization when using the Doppler effect. The same symptoms during sonographic examination in children with AHO in the early period were indicated by other authors [13-15]. We completely agree with the opinion of German scientists [8], who drew attention in their scientific work to the importance of the subjective opinion of the doctor conducting the ultrasound examination. Blood cultures for sterility were performed once in patients with high fever and other general manifestations of the disease. In all observations there was no pathological growth of microflora.

In the control group, 21 (31,3%) patients had intraosseous pressure measured (Waldman test) on the first day of the child’s hospital stay. Bone perforation was carried out in the diaphyseal part of the bone or at the border of the metaphysis and diaphysis. However, the Waldman test was not always

positive. In our opinion, there may be several reasons: 1) the predominance of the pathological process in the metaphyseal part of the bone; 2) slow development of the pathological process in the intramedullary phase, as a result of which the amount of intraosseous inflammatory fluid was not formed in sufficient quantities; 3) errors in the research. One way or another, this study is carried out under general anesthesia in an operating room, when a clinical diagnosis has already been made and surgical intervention is required. For the purpose of differential diagnosis of AHO of long bones, the authors did not measure intraosseous pressure as an independent method in our hospital. We do not agree with the opinion of some authors [10], who consider the Waldman method to be the key to successful diagnosis of AHO. On the contrary, we consider the measurement of intraosseous pressure a historical milestone in the diagnosis of AHO.

Bacterial culture of discharge from a perforation hole in the bone allowed in most cases to identify *Staphylococcus aureus*. In 13 (19.4%) patients of the control group there was no growth of microorganisms on the nutrient medium. Methyl-resistant strains of *Staphylococcus aureus* were diagnosed only in 4 (5.9%) cases. In other cases, associations of microorganisms, *Staphylococcus epidermidis* and some other bacteria were sown.

We took into account the results of the analysis of ongoing research activities in creating a diagnostic algorithm for patients in the main group. An MRI examination of the affected limb was performed in 33 (55%) patients over 10 years of age. Children of this age group could perform this study without the use of anesthesia. Some of them required the presence of one of the parents in the study premises. We consider MRI to be a very effective method for studying AHO in the early stages. The following diagnostic criteria were defined: thickening of the periosteum, the presence of pathological hydration (trabecular edema in metaphyseal localization, increased volume of intraosseous fluid, soft tissue edema, synovitis of nearby joints, the appearance of fluid in the intermuscular spaces) on T1-weighted and T2-weighted images. The data obtained indicate the presence of inflammatory changes in the limb segment. Half of the patients who underwent ultrasound examination showed signs indicating an inflammatory process in bone tissue [15-16]. When performing osteoperforation of the affected area of the bone in all patients of the second group, in addition to a smear of the contents of the bone marrow canal, the authors took a small area of the affected bone tissue from the site of the suspected pathological process and sent it for microbiological examination. This made it possible to inoculate pathological bacteria in all observations, incl. methyl-resistant strains of *Staphylococcus aureus* in 11 (18.3%) patients.

In addition, for the treatment of acute hematogenous osteomyelitis in the metaphyseal zone of long bones, we have developed and tested a new method of surgical treatment, which has been shown to be effective in combating the chronicity of the pathological process.

The introduction of the presented algorithm into the work of the pediatric surgery clinic in 2019 made it possible to reduce the complicated course of acute hematogenous osteomyelitis in the form of a transition to the chronic form to 10%, and the number of chronic forms of hematogenous osteomyelitis among patients with metaphyseal localization of the pathological process was reduced to zero. In the second group, only 3 (5%) patients were diagnosed with a chronic course of hematogenous osteomyelitis in the projection of the diaphyseal part of the bone.

### Conclusions

1) The use of the proposed algorithm for diagnosis and surgical treatment made it possible to reduce the complicated course of AHO in the form of transition to a chronic form to 8,3% ( $p=0,048$ ), and the number of "chronicles" among patients with metaphyseal localization of the process was reduced to zero;

2) We consider MRI, especially in children with metaphyseal localization of the pathological process, and MBI of the bone fragment to be the most effective methods for early diagnosis of AHO of long bones;

3) X-ray, SCT, ultrasound of the limb and Waldman's test are of little significance and are ineffective in the early period of the disease;

4) We consider early osteoperforation and bone drainage, as well as correctly selected and long-term antibiotic therapy, to be the main method of treatment for AHO of long bones;

5) The use of a new method of surgical treatment of patients with metaphyseal localization of the pathological focus in long bones is a promising method that requires further study.

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