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TRICHINELLOSIS IN MAN AND ANIMALS. THE RECENT ACHIEVEMENTS IN THEORY AND PRACTICE

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Although trichinellosis is actually ancient and severe helminthic disease in man and animals, the knowledge of it is not equal in different parts of the world. Since recently the problems of trichinellosis have been paid due attention in Europe and the North America (mainly in the USA and Canada), while in the South America, Africa, and the major part of Asia inhabited by two thirds of the world population, the knowledge of trichinellosis is inadequate. This paper presents the modern state of knowledge on the fundamental problems: habitat — wild and domestic carnivorous animals — man, and the measures for preventing the dangerous disease.

Introduction

Trichinellae, causing trichinellosis in man and animals, are thought to have been adapted to parasitizing in birds and mammals several millions years ago, about the Miocene, and Trichinella ancestors seem to have lived in predatory dinosaurs in the Middle and Late Cretacious. Trichinellae are cosmopolitan and parasitize in carnivorous mammals world-wide Human beings became susceptible to trichinellae infections since they had began to consume meat. Indeed, cases of human trichinellosis were more frequent before the usage of fire than later on, when meat products were mostly eaten after thermal treatment. In that ancient time when man consumed meat obtained exclusively by hunting, the

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only source of trichinellae infections were wild carnivorous mammals (bears, wild boars, some species of canines, felines, and pinnipeds). Perhaps, at the very beginning of human race formation, people became aware of a severe disease caused frequently by consumption of meat of wild predatory mammals from canine, feline, and hyena families, which are also highly infected with trichinellae at present. This observation seems to cause an almost universal custom to regard the meat of the above species as inedible. Natural sources of trichinellae to man remain crucial up to now.

After domestication of swine some 7 thousand years ago, the danger of human trichinellosis increased. However, the danger was very slowly realized. Gould [1] reported that in 1288 B.C., during the reign of Rhamses II, the Prophet Moses forbade the Hebrews to consume pork, the reasons supposedly being *Trichinella* and tape worm invasion. Indeed, although people had no actual notion of trichinellosis at that time, the cases of a severe disease following the consumption of pork were generally known. Two thousand years later Mohammed introduced the same control measure for Mohammedians. The rest of the civilized world began checking pork for trichinellosis only in the second half of the XIX century, after the discovery of *Trichinella spiralis* Owen, 1835. It was not long ago that human trichinellosis was frequent in the Western Europe and in the USA. From 1860 to 1926 in Germany 16 541 cases of human trichinellosis including 809 lethal cases were recorded. During about two decades before the second world war the extensive measures against trichinellosis were taken in the country. These measures were based on total inspection of pork for trichinellae and destruction of infected carcasses. The simple but rigorous measure lead to almost absolute elimination of swine trichinellosis and decline of human trichinellosis. During second world war the number of trichinellosis cases in Germany and other fighting countries increased because of loose controls and extensive migrations of people and animals. The trend persisted during the years following the war. A number of authors [2-4] reported several outbreaks of human trichinellosis: from 1947 to 1959 with more than 1000 cases, and from 1966 to 1973 with nearly 4000 cases.

Kagan [5] noted that in the first half of this century some one fourth of the USA population were infected with trichinellae. The overwhelming majority of human trichinellosis cases were due to pork consumption. The rate of trichinellosis in swine varied from 0.3 to 11 per cent, which resulted from the lack of compulsory trichinoscopy regulations and from feeding swines with garbage without preliminary decontamination. With cheap pork produced in the USA for export, *T. spiralis* was introduced into many American and European countries. The rate of swine trichinellosis dropped after the adoption of legislation according

to which garbage must be cooked before feeding to swine. However, the problem of trichinellosis is not completely removed in the USA. Hill et al. [6] reported that in Illinois 0.13 per cent of slaughtered swines were infected with trichinellae and in some farms the rate of infection was as high as 50 per cent.

According to Bessonov [7] 11 963 cases of clinical human trichinellosis were recorded from 1946 to 1967 in the USSR, with 83 per cent of the cases in the BSSR. The main source of infection was the pork from home slaughter which was not subjected to veterinary or sanitary inspection. Infections from wild animals accounted for only 2.9 per cent during the same period. The trichinellosis situation in the USSR has somewhat changed during the last 15 years. The number of synanthropic trichinellosis cases decreased and that of sylvatic trichinellosis increased.

In 1960, the International Comission on Trichinellosis was established with the purpose of consolidating the efforts for struggle against trichinellosis. An invaluable role in coordination and intensification of the work of the Commission was played by its first General Secretary, Professor Z. Kozar. Six International conferences on major aspects of trichinellosis problem have been held by 1985. The period highlighted three major developments: the world-wide occurrence of trichinellae in wild and domestic animals has been recorded; three new species of *Trichinella* have been described, and the third, but not the least, thiabendazole, a highly effective anti-trichinellae drug, has been synthesized.

Brief description of trichinellosis agents

By now four species of Trichinellae have been described: *Trichinella spiralis* Owen, 1835; *T. nativa* Britov, Boev, 1972; *T. nelsoni* Britov, Boev, 1972; *T. pseudospiralis* Garkavi, 1972.

Each of the *Trichinella* species is reproductively isolated and differentiated from the others by a number of characters.

Trichinella pseudospiralis. The species was first found in the North-American raccoon, *Procyon lotor*, from the North Caucasus. In terms of evolution it is the most ancient species of the genus. It is the only representative of trichinellae, parasitizing in birds.

Adult females are 1.26-2.10 mm long and 0.029-0.035 mm thick. Males are somewhat smaller than females. Larvae localize in muscular fibers. Infective larvae are ca. 700 μm long. Larvae are not encapsulated in any host species. They become infective in 17 days after infection of mice. The infective larvae are highly sensitive to freezing and lose infective capacity after two days at −10°C. In addition to birds, the species can parasitize in swine, fox, raccoon, dog, rodent, and bear. In dogs larvae, die shortly after penetration into muscle. The area of the species is not definitely outlined as yet. However, with the larvae sensitive to freezing,

the species can not occur in the regions with cold winter. High susceptibility of birds to *T. pseudospiralis* may suggest that the species is distributed in subtropical and tropical regions abundant in birds feeding on carrion (India, Africa, and the South America).

Trichinella nelsoni. The distinctive features of this form was noted by Nelson and Rickman [8] while studying the trichinellae isolated from people infected through consumption of wild boar meat. The species is of later origin as compared with *T. pseudospiralis* but it is difficult to state whether the latter is the immediate ancestor of the species. But *T. nelsoni* seems to be the first of the presently known encapsulating species of *Trichinella* and is considered a parent species of the next two encapsulating trichinellae.

Adult males are 1.3-1.5 mm long and 0.3 mm thick in the thickest posterior part of the body. Females are twice as large as males. Infective larvae are ca. 1 mm long. In host muscle, the larvae are encapsulated. The larvae become infective 20 days after infection of mice. The infective larvae are highly sensitive to freezing and die within 4 to 7 days at 10 to 12°C below zero. It parasitizes in wild carnivorous mammals of Africa, India, and of the South-West Euroasia south of the 45°N, but in the region influenced by the Gulf Stream and by its continuation, the North-Atlantic Current, *T. nelsoni* area expands up to nearly 63°N. There are no records of the species in the Soviet Far East and in the South America.

Trichinella nativa. Originally the form was described as a separate biological unit in 1969, basing on the results of genetic, morphological and physiological studies, later it was described as a variety and then raised to the species rank. The essential anatomic features of *T. nativa* are similar to those of *T. nelsoni*, the latter being the parent species. The larvae become infective in 17 days after infection of mice. Rounded capsulae are formed around the larvae in the host muscle. The parasite is well adapted to canines and felines but poorly adapted to rats and swines. Encapsulated larvae are highly tolerant to freezing. They remain infective for 1.5 years at 10°C below zero, and for one month and more at 20°C below zero. Due to the low temperature resistance *T. nativa* is spread all over the Holoarctic region up to the North Pole but it was not found south of the 40th parallel.

Trichinella spiralis. In terms of evolution the species is the last in the genus. It branched from *T. nelsoni* some 7 thousand years ago during wild boar domestication and evolved during subsequent swine breeding. Morphologically the species closely relates to *T. nelsoni.* It parasitizes in synanthropic animals: swines, mouse-like rodents, and domestic cats, and can infect wild predatory mammals. The species has no definite area and its distribution relates to economic activity of man, primarily due to swine breeding. The larvae are sensitive to freezing.

Identification of *Trichinella* species

Identification of *Trichinella* species is of utmost importance for sanitary and preventive measures in trichinellosis foci. Workers of applied veterinary and medicine should have accurate knowledge of an infective agent, source of the agent, its characteristics, and the level of tolerance to various factors of environment. Information on specific affiliation is the first and necessary condition in conducting scientific studies on trichinellae. Lack of such information leads to the situation when the results of studies conducted by a worker may bewilder another worker using the same methods but dealing with a different species of the genus.

Now that we have profound knowledge of each *Trichinella* species, the identification of the species became easier. Morphologic and adaptation criteria can be used for this purpose. *T. pseudospiralis* is easily identified by morphological features. The species larvae do not encapsulate, the larvae and adult worms are 30 per cent smaller compared to encapsulating trichinellae, the species is well adapted to birds and completes its life cycle therein.

T. spiralis larvae enclose themselves into elongated oval capsulae (Form index 1.48-2.70) upon 8 months from infection of animals. Some 26 per cent of males have intestine along the concave side of the body, like in females, but with a long (50 μm) rectum. Other encapsulating trichinellae include only 3 to 5 per cent of such males.

T. spiralis larvae become infective in 19 days after infection of mice. The species is well adapted to swine, rat, and rabbit, in the muscles of which they remain infective lifelong. In 30 to 40 days post infection the quantity of dying larvae in the muscle of the animals is 2 per cent or less. In meat the incapsulated larvae die in 4 to 7 days at 10-12°C below zero.

T. nativa larvae form rounded capsulae (Formindex 1.20-1.30) in 3 to 8 months after infection of animals. The larvae become infective in 17 days after infection of mice. The parasite is well adapted to canines and felines, and poorly adapted to rat, swine, and rabbit. Fifty to sixty per cent of muscle larvae die in 30 to 40 days after infection of swines and rats. Total breakdown of the species larvae is completed in swine muscle in 130 to 150 days, in rat muscle in 4 to 6 months, and in rabbit muscle in 1.0 to 1.5 years. Complete breakdown of the larvae takes longer periods only in young animals with heavy invasions of 1000 and more larvae per gramm of muscle. In meat the species encapsulated larvae remain infective during 9 to 14 months.

T. nelsoni become infective in 20 days after infection of mice. The extent of *T. nelsoni* adaptation to animals is similar to that of *T. nativa* while its low temperature resistance is comparable to that of *T. spiralis*.

Valuable scientific results can be obtained by crossing a detected *Trichinella* isolates with the standard species. The criterion for species identification in crossing tests would be normal reproductive progeny.

As soon as the three new species of *Trichinella* had been described, controversy between adherents and opponents of the concept of polyspecificity arose. This resulted from a number of reasons, the principal ones being as follows: firstly, (a psychologic barrier) opposition to new species is to a great extent determined by the authority of the world's leading parasitologists who during 135 years supported the idea of monospecificity of the genus; secondly, all encapsulating trichinellae have similar morphologic characters while the criterion of morphologic similarity dominates in helminthologic diagnoses; thirdly, some authors just did not see any advantage in recognizing polyspecificity of *Trichinella* genus. Though the latter reason is far from being scientific, it was not the least in creating the situation.

Any investigator who is not sure about the validity of the three new species can satisfy his doubts using simple and easy methods (a test for *Trichinella* sensivity to freezing and for adaptation to rat and swine). Duran et al. [9] reported a distinct difference in larvae fatty acid composition in all encapsulating trichinellae. A crossing test is a tedious method but it brings the most convincing results and a great satisfaction to a researcher perceiving the truth. Of course, crossing tests should be done with great care not to get erroneous results.

From the above information the reader can easily get some idea of the areas of trichinellae. A low temperature resistant species, *T. nativa*, is distributed through the Holoarctic region north of 40°N. *T. nelsoni* and *T. pseudospiralis*, being thermophils, occur in geographic regions with mild climate. In the West Europe *T. nelsoni* area extends north up to 63°N while in Asia its northern border coincides with 45°N. *T. spiralis* has no definite area and its distribution is related to economic activity, namely to swine breeding. In wild animals the species parasitizes extremely seldom and only in the regions with mild climate.

The three encapsulating trichinellae are human trichinellosis agents. Taking into account the fact that simians and many other mammals are easily infected with *T. pseudospiralis* it may be assumed that man is susceptible to invasion of this parasite. *T. spiralis* is characterized by the highest degree of adaptation to man, whereas the degree of adaptation of *T. nelsoni* is lower. This observation is of great importance for treating clinical patients, as discussed later. Man is exposed to trichinella infection only when consuming raw or undercooked meat and meat products.

Clinical symptoms and patogenesis of Trichinellosis

Some authors [10-12] describe human trichinellosis as manifestating in fever, intoxication, and allergic syndrom. The severity of the disease is directly related to quantity and quality of the invading agent. Significant doses of highly virulent trichinellae result in severe course of the disease with a short incubation period, explicit clinical signs, detrimental pathology of internal organs, and high percentage of lethal outcomes. On the other hand, small doses of low virulent trichinellae cause a weak response of an organism, the course of the disease is often asymptomatic and without apparent pathology.

Clinical signs of human trichinellosis become usually evident at an invasion rate of 25-50 larvae per gramm of muscle. In adult man this rate of invasion develops after the dosage of 50 000 of *T. nativa* larvae. Aged 2 to 4 months *T. spiralis* larvae from swine have the highest virulence for man, and dose resulting in distinct symptoms of trichinellosis can be much less. In addition, *T. spiralis* larvae are two times more fertile than *T. nativa*. Old larvae of *T. nativa* and *T. nelsoni* even from main hosts (bear, badger, warthog, walrus et al.) have low virulence due to predominance of males and to lowering larva viability as a result of their ageing. Indeed, this is true for *T. spiralis* as well, but normally swines are slaughtered when young, and old trichinellae are rare in pigs.

In the patogenesis of trichinellosis, a general resistance of man at the time of invasion is important. Impaired resistance, regardless of its cause, contributes to more intensive invasion due to higher percentage of trichinellae establishing in the intestine, prolonged intestinal phase of the infection, and lower percentage of growing larva mortality in the muscle. In the light of the abovesaid the age factor should be also pointed out. Children are more susceptible to trichinellae, and the disease symptoms show up in them from much less dose of the infection.

A comparatively mild course of trichinellosis is observed at invasion intensity of up to 250 larvae per gramm of muscle. At the rate of 260 to 500 larvae per gramm of muscle the disease is characterized by a moderate course. The higher rate of invasion results in severe trichinellosis. When not aggravated with other diseases, and without specific treatment trichinellosis is lethal to man at invasion rate of 1 to 2 thousand larvae per gramm of muscle. After invasion of very significant quantity of highly virulent agent (300 thousand and more larvae per adult man) the disease may be lethal during intestinal phase of *Trichinella* infection, one to three weeks post infection. In these cases incubation period lasts 6 to 8 hours and is followed by gastro-intestinal disturbances: frequent mucous, later bloody stools, colic, nausea, vomiting. These are accompanied with

desquamation of small intestine epithelium. Body temperature rises up to 39-40°C. There appear symptoms of nervous and cardiovascular system disorders due to intoxication with intestinal *Trichinella* metabolites and infiltration of products of incomplete enzymolysis through the naked mucous membrane of intestine. Organism dehydration caused by diarrhoea, and penetration of intestinal microflora into blood aggravate the course of the disease, and it may be complicated by sepsis. Later, 2-3 weeks post infection, in addition to the signs described above, myositis, eosinophilia, pneumonia, and myocarditis involve. Intoxication results in liver lesion. The symbionts of trichinellae, staphylococci, play a role in the disease pathogenesis. They are present in all tissues of the parasite, and pass to the next generation transovarially. *Staphylococcus* infection complications manifest in increasing pain in skeletal muscles, skin eruption, suffocating, and oedema of face and extremities. An allergic component of the disease may contribute to oedema but is not the major factor of it as some workers believe. The major factor of acute trichinellosis is toxicosis caused by Trichinella metabolite infiltration and, undoubtedly, by toxins of staphylococci, the *Trichinella* symbionts. Tests on experimental animals show that i.v. injections of the culture of *Trichinella* symbionts result in symptoms of severe trichinellosis with intestine, lung, liver, and skeletal muscle lesions.

When agent doses are moderate the above signs of the disease are weaker and incubation period is longer. With *T. nativa* the above signs maintain for 3-4 weeks and more due to constant mortality of *Trichinella* larvae in muscle, and chronic poisoning. Such a prolonged duration of the disease is not characteristic of infections with *T. spiralis*. Without treatment the disease ends in gradual recovering and elimination of clinical signs during 6 to 7 weeks postinfection. During this period larvae encapsulate and poisoning ceases. The course of the disease is aggravated when patients are prescribed cortison, prednisolon and similar drugs because the hormones, far from killing the agent, really promote prolonged parasitizing of intestinal trichinellae and increase invasion intensity several times by inhibiting immunogenesis, inflammation, interferon synthesis and other features of the host's protective responses. In such cases trichinellosis became chronic. Normally trichinellae live in intestine of man 3 to 4 weeks, rarely 5 weeks. When patients are prescribed cortison and prednisolon, intestinal trichinellae reproduce during 15 to 16 weeks.

A chronic phase of trichinellosis occurs also when the disease agents are *T. nativa* or *T. nelsoni*. When the patients do not get specific treatment, gradually dying out larvae maintain staphylococcus infection and chronic poisoning. High and prolonged eosinophilia is common in such cases.

Diagnosis

Clinical symptoms of trichinellosis include following diagnostic signs: general weakness, malaise, digestive disturbance, abdominal pain, eosinophilia, then myalgia; pain appearing with eyeball and tongue movements, face and extremity oedema, skin eruption. Stating fact of consumption of raw or undercooked meat of trichinellous animals is highly important for diagnosis. Detecting *Trichinella* larvae in the meat remains is decisive in such cases. Reliable data are obtained with ring precipitation test as well as latex agglutination test, double diffusion test and complement fixation, especially when these tests are used in complex. But the most quick and accurate diagnosis is obtained from examination of a biopsied piece of a skeletal muscle, usually musculus brachialis.

Biopsy brings the most rapid and accurate evidence. Detection of larvae or their traces is the major criterion of diagnosis. In addition, intensity and duration of infection are estimated and *Trichinella* species involved is roughly identified (poor cell infiltration and the absence of dead larvae are characteristic of *T. spiralis*, and the presence of dead larvae and massive cell infiltration of muscle tissue are characteristic of *T. nativa).*

A low intensity of muscle invasion associated with high eosinophilia usually suggests *T. nativa* infection. This is due to larvae destruction and release of the symbionts (*staphylococci*) resulting in higher eosinophilopoiesis. In infections with *T. spiralis*, the species most adapted to man, this sharp discrepancy between the intensity of invasion and eosinophilia is rare. Some clinicists argue against biopsy, the arguments however being groundless, because biopsy even from internal organs is frequently used in applied medicine and always used when malignant tumor is suspected.

Treatment

A great number of drugs were tested for a possible trichinellocidal effect with no positive results in the majority of cases. In fact, there had been no specific drug against trichinellosis until thiabendazole appeared. Patients were treated just symptomatically. Extensive use of cortison and prednisolon began in 1948 and these drugs were used in treatment of trichinellosis. These antiinflammatory drugs, when used during the first week or at the peak of the disease, remove some clinical signs and temporarily improve the patient condition, producing false impression of positive therapeutic effect.

Cortison was introduced into applied medicine without preliminary

tests on animals and its negative effects were revealed during clinical practice. The use of glucocorticoids in trichinellosis treatment became as widespread as their use in the treatment of rheumatoid artritis and allergy. It must be noted to the credit of many biologists that there began simultaneous detailed testing of cortison in investigations on animal trichinellosis. It was immediately shown that usual therapeutic doses of cortison used during first two or four weeks after infection increase the invasion intensity 4 to 12 times as compared with control animals, suppress immunity development and increase mortality.

Corticosteroids have low molecular weight (ca. 300) easily penetrate cell membranes and can interact with nucleus receptors. They act to destroy the majority of thymus cortex lymphocytes. Diminishing cell macrophage function, the drugs prevent spontaneous mortality of poorly adapted to man *T. nativa* and *T. nelsoni* larvae and slow down their phagocytosis.

As a result of steroid therapy, gastro-intestinal disorders acute gastric and intestinal ulcers, severe vasculitis accompanied by hemorrhages and necrosis, myocarditis and progressing mental disorders are observed in patients. In most cases death ensued as a result of cardio-pulmonary arrest or profuse gastrointestinal bleeding. In these cases sepsis usually develops due to staphylococci. It follows from the above evidences that corticosteroid hormones are counterindicative in treating trichinellosis.

Thiabendazole and its derivatives have strong trichinellocidal effect. Unlike cortison, thiabendazole had been thoroughly tested on animals for a long period of time and only then applied in clinical practice. It was introduced into medicine from veterinary practice, where it was tested on several million animals of different species. Thiabendazole metabolites have low toxicity in mammal organisms. Some 85 per cent of orally administered dose of the drug is excreted with urine and to a lesser extent with faeces during 72 h after intake [13, 14].

The sequence of thiabendazole effect on trichinellae is as follows. Small doses of the drug first obstruct *Trichinella* embriogenesis not affecting other vital processes in adult parasites. Higher and prolonged thiabendazole dosage disrupts metabolism in adult trichinellae and leads to their death. Growing larvae are highly sensitive to the drug and die at any stage of development. Larvae dying at preinfective stages are subjected to autolysis and phagocytosis with a minimal number of phagocytes. Infective larvae, especially when encapsulated, are more resistant to the drug as compared to embryos and growing larvae. Under an influence of thiabendazole they stretch (larva body is mostly peripheral in the capsule) and loss the ability to coil when cooled, though they remain alive; muscular paralysis is very probable. Cuticle becomes permeable for chemical substances, particularly for HCl molecules. Soon

such larvae die and undergo autolysis. The first signs of enzymolysis show on the larva head end, then the process involves esophagus down to the cell body and alimentary tube including reproductive organs. The cell body and cuticle are destructed the last. Change of intracapsule sarcoplasm takes place along with larva autolysis. The enlarged muscle nuclei gradually become lighter in colour, nucleoli first enlarge but then wrinkle or break into small granules. Sarcoplasm transforms into amorphous eosin-stained substance, consisting of minute lumps, which later merge to form larger lumps, with frequent formation of vacuoles. Upon dying off of intracapsular sarcoplasm the capsule and larva undergo cell infiltration. At first neutrophils, eosinophils, and histiocytes prevail in the infiltrate. They rapidly increase in number. Capsule walls are loosen, cells penetrate capsule through resulting cracks, and phagocytosis of larva begins. From the moment phagocytic resorption of the capsule proceeds both from outside and from inside. With the process of cell breakdown of larva and capsule fragments, the infiltrative and proliferative cells undergo transformation. Neutrophiles, eosinophiles, and histiocytes are succeeded by plasma, epithelial, and giant cells with few lymphocytes among them. Typical parasitogenic granulomae are formed, three to four times as large as larva capsules. On completing the function of phagocytosis of larva and capsule fragments the granuloma cells die and resorb leaving no traces of invasion. Sometimes in the centers of large granulomae, particularly where larva breakdown was incomplete, necrotic foci are formed with subsequent deposition of calcium salts.

Larva resorption is followed by muscle tissue regeneration. In a great majority of cases the morphologic regeneration of muscle is complete. As far as tissue sarcolemma is not disrupted by parasitizing larva, and muscle sarcolemma does not subject necrosis, fiber structure regenerates comparatively soon after the phagocytosis of dead larva. Only rarely, when phagocytosis of larvae and old large capsules is incomplete, the centers of parasitogenic granulomae are calcificated to some extent and muscle tissue remains defective for a while.

Analysis of the dynamics of dying off and breakdown of larvae under the influence of thiabendazole suggests that the drug affects the parasite metabolism. The more intensive are the processes (in embryos and growing larvae), the more they are sensitive to the drug, and on the contrary, low metabolism stage (encapsulated larvae) is less sensitive to it. Nevertheless, trichinellosis has proved to be curable, and applied dosage of thiabendazole is comparatively harmless for man and animals.

Thiabendazole seems to have been introduced into clinical practice since 1963. In 1964 three reports on thiabendazole positive effect in human trichinellosis treatment were published in the USA. Soon the medical preparation came into use in other countries. For example, in Poland it

was found that thiabendazole immediately affects encapsulated larvae of trichinellae in man and causes the death of the helminth and also increased phagocytic response in muscle tissue. The applied dosage was 25 to 60 mg per kilogramm of body weight during 3-5 days irrespective of the stage of the disease.

In the USSR thiabendazole has come into clinical practice since 1969. Since then we observed more than 100 patients suffering different stages of trichinellosis caused by either *T. spiralis* or *T. nativa* invasion. Provisional clinical diagnoses (serum diagnoses in several cases) were confirmed by biopsy from skeletal muscles, mostly from musculus brachialis. Biopreparations from 36 patients were examined before or after treatment. Two patients underwent biopsy before as well as after treatment.

The range of invasion varied from 1 to 3100 trichinellae per gramm of muscle. As a rule severe trichinellosis was observed at invasion intensity of 500 and more larvae per gramm of muscle. Some 40 patients took prednisolone and hydrocortisone for 2 to 6 weeks according to the existing directions. But in the most cases the disease grew progressively worse. In these cases thiabendazole (minthezole) was prescribed on corticosteroid therapy background, which reduced treatment efficiency. When the drug was prescribed to patients before day 20 of infection and without corticosteroids, a complete recovery was observed even at invasions of high intensity. For example, in a patient with an invasion intensity of 3100 growing larvae of *T. nativa* per gramm of muscle at day 18 post infection a majority of muscle fibers were involved in the process (myofibrille enzymolysis and helminthic myositis). The patient was in extremely bad condition, but after 12 days of minthezole therapy with a dosage of 500 mg (by active substance) 2-3 times a day the patient began to recover. In a week he was able to get up and walk without help. Biopsy from the right musculus deltoideus was repeated in 45 days after the end of the treatment. *Trichinella* larvae were not detected in either native sections or histologic preparations. Regeneration of muscle tissue was complete. In five months after the end of treatment the patient had no complaints, his working capacity and muscular strength of body and extremities completely restored.

In patients with the majority of larvae encapsulated (i.e. 30 to 60 days post infection) minthezole therapy gave favourable results. Control biopsy made after 14 days of minthezole treatment showed 97 per cent larva mortality, with larvae undergoing cell enzymolysis and phagocytal resorption. When the treatment began later, the clinical effect was also pronounced but recovery slowed down. This seems to be due to slow resorption of adult larvae and their capsules.

Along with minthezole, neomycine, antibiotics to which staphylococ-

cus symbionts are sensitive, and staphylococcus antiphagin or immunoglobuline were prescribed. When invasion was heavy, intensive desintoxication therapy was applied.

Recently new and highly active preparations, such as decaris and gentomycin have appeared. These new drugs have favourable therapeutic effect and accelerate recovering. Decaris paralyses the muscle system of intestinal trichinellae and promote their expelling from the intestine. Complete intestinal dehelminthization is achieved during first 24 h period of treatment. The drug should be prescribed immediately when acute trichinellosis is suspected. But decaris does not kill larvae, therefore the patient should be treated with either minthezole or vermox and/or other drugs — thiabendazole derivatives. Gentomycine is the most active antibiotic affecting staphylococci and its use on the background of trichinellocidal drugs prevents the development of staphylococcus infection and organ lesion.

Thus, thiabendazole (minthezole) application in dosage of 500 mg 2-3 times a day during 9-12 days kill intestinal, growing and encapsulated trichinellae. However, it should be remembered that *T. spiralis* (as the most adapted to human organism) is more resistant to the drug and it should be applied in maximum dosage for a prolonged period. It should be noted that in the period of mass breakdown of larvae large quantities of foreign protein and staphylococcus symbionts of the helminths enter patient's blood and result in transitory aggravation of symptoms. But proper (simultaneous with thiabendazole) application of antistaphylococcus preparations, cardiac medicines, and drugs of detoxicating and roborant effect would alleviate or prevent the aggravation development.

According to available information thiabendazole was used for treatment of trichinellosis in more than 350 patients with no lethal outcomes in spite of transient aggravation symptoms. Meanwhile, from 150 patients treated with corticosteroids 6 died, in many patients the disease became chronic, and in some patients ulcer lesions of gastrointestinal tract developed.

Thus the available evidence is indicative of lack of efficiency and, when improper applied, of harmfulness of corticosteroid therapy in treating human trichinellosis. The most effective preparations against the disease are thiabendazole and its derivatives. Decaris is effective against intestinal trichinellae. The course of treatment of an adult man infected with *T. nativa* through consumption bear's flesh shashlyk (incubation period of three weeks, invasion intensity of 500 larvae per gramm of muscle) was as follows: decaris, 150 mg, twice with 8 h interval; moderate doses of gentomycin or monomycine, intramuscularly, for 12 days; minthezole (thiabendazole) (in 4-6 h after intake of the second

dose of decaris), 500 mg (by active substance), twice a day during morning and evening meals for 10 days. Application of staphylococcus antiphagine or immuno-globuline is desirable in the middle of the course of treatment, and detoxication measures should be applied when the condition of a patient requires. Glucocorticoids are counterindicative.

Immunity

Upon suffering trichinellosis human beings and animals acquire high specific immunity, which maintains practically lifelong. The level of immune activity depends on severity of the disease and is not associated with the presence of larvae in host's muscle (sterile immunity may occur). Immunity acquired against one species of *Trichinella* is effective against other trichinellosis agents. The second case of trichinellosis in the same person occurs extremely seldom.

As in other helminthiases, immunity against trichinellosis is of cellular nature and its induction is related to the intestinal phase of the disease. Stable immunity is generated as a response to metabolites of intestinal trichinellae, therefore in case of repeated infection the immunity manifests itself in small intestine, i.e. at the primary spot of invasion. Immune reactions of an organism are quickly mobilized, they are of allergic nature. The reaction of *Trichinella* expelling is based mainly on the inflammation of sensitized intestine. At reinvasion, the phagocyte cells, especially polymorphonuclear leucocytes, accumulate in the intestinal wall on the background of intense hyperemia and cause complete expelling of trichinellae. Immune reaction can be dramatically decreased or even totally eliminated by X-ray irradiation or exposure to corticosteroids or other immunodepressants [15].

All natural phenomena are correlated and interrelated, this is also seen in host-parasite relations at trichinellosis. We will indicate only two aspects in immunologic characteristics of a host, who has suffered trichinellosis. Firstly *Trichinella* antigens have common determinants with many other helminths, protozoan, and bacteria, therefore the host with intense immunity against trichinellae maybe simultaneously resistant to these invasions and infections. Secondly, stimulating a host's immune system, trichinellae support it at a high level thus promoting its main mission — maintaining genetic stability of an organism internal environment in variable external environment. A number of authors [16-18] showed that animals with immunity against trichinellae are comparatively more resistant to malignant tumors and amoebic abscess of the liver.

Prophylaxis and control

Prophylaxis of human trichinellosis is very simple: consumption of raw or undercooked meat of trichinellous animals (swine, boar, bear, walrus, seal, raccoon, raccoon dog, fox, etc.) not examined by sanitary/veterinary services should be avoided. It should be noted that *T. nativa* larvae are cold-resistant and freezing of meat in home refrigerator is no prophylactic measure against trichinellosis. Invasion becomes possible only when the rule is broken. But even then the development of the disease can be prevented, if within 5-6 days after consumption of trichinellous meat, when general malaise and stomach upset set on, a physician is advised. Though it is really difficult to diagnose trichinellosis in this initial period, the disease can nevertheless be recognized through studies of suspected meat and patient's feces. In case of grounded suspection of trichinellosis it suffices to prescribe the patient two 150 mg tablets of decaris to prevent the development of the disease. The process would stop in the intestinal phase but the immunity against trichinellae would have been already acquired. Preventive measures against trichinellosis are implemented mainly by veterinary service. Its mission includes identification of the agent, detecting the source of infection and eliminating the latter, and organisation of slaughter of potentially trichinellous animals in abbatoirs and other slaughter places with obligatory trichinoscopy of every carcass according to antitrichinellosis regulations. It is important to inform population of measures to be taken against trichinellosis.

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