

Paper 40

Clinical, Epidemiological and Parasitological Features of the *Trichinella* strain (ATS)

N. N. OZERETSKOVSKAYA and YE. V. PEREVERZEVA

Institute of Medical Parasitology and Tropical Medicine, Ye. I. Martynovskiy Ministry of Public Health USSR, Moscow.

INTRODUCTION

The problems of the taxonomic individuality of natural arctic *Trichinella* strain (ATS) attacks (in connection with the phenomena of the clinical epidemiological peculiarities of trichinosis in humans produced by this strain) have been studied (Ozeretskoykaya and Uspenskiy 1957; Ozeretskoykaya 1956, 1968). Further, there has been established a sharp destruction of the process of encapsulation in muscle of larvae in humans and their massive kill in the course of the first months of invasion (Ozeretskoykaya *et al.* (1966). The experimental study of ATS from the polar bear (*Thalarctos maritimus*) on Franz Josef Land showed a stable, low invasibility of ATS for laboratory rodents and higher sensitivity to specific chemicals in comparison with the laboratory strain of *Trichinella* (LST), obtained by prolonged passage of synanthropic (pig) strains of *Trichinella* in laboratory rodents. The method of disc electrophoresis in polyacrylamide gel also established that there were peculiarities of protein content of ATS larvae and protein shifts in blood serum caused by strains invasive for laboratory animals in comparison with LST and certain other strains of *Trichinella* (Ozeretskoykaya *et al.* 1969a, 1970).

On the basis of reproductive isolation tests, laboratory strains of *Trichinella* were initially distinguished from those from domestic animals of synanthropic foci, from wild mammals of the European and Asiatic parts of the Soviet Union, and from predators of the African continent (Britov 1971). A position was advanced based on the presence of three varieties of parasite, which were further elevated to the rank of species (Britov and Boyev 1972). Along with ATS, native strains of *Trichinella* from wild mammals of all parts of the Eurasian and North American continents were added to *Trichinella nativa* sp. nova. At the same time the native African strain from hyenas was named *Trichinella nelsoni* sp. nova and was also discovered in the southern Ukraine (Britov and Boyev 1972). Later, evidence was produced regarding the possibility in interbreeding these enumerated three strains of *Trichinella* (Komandarev 1973; Meerovitch 1973, pers. comm.; Bessonov 1974).

CLINICAL EPIDEMIOLOGICAL FEATURES OF ATS

We studied 242 cases of human trichinosis of which 18 cases of infection were caused by ATS. In 15 patients the disease was contracted from the meat of the brown bear (*Ursus arctos*); seven cases in arctic and subarctic areas of the European continent; eight cases in the Asiatic parts of the Soviet Union. Three patients contracted trichinosis from the meat of the polar bear of the Novosibirsk Islands. Among the remaining 224 patients, 140 were from endemic foci of trichinosis in Western and Central regions of the European part of the Soviet Union. In 84 cases, the infection was caused by native strains of

Trichinella passed through domestic swine (STS). Of the 84 patients, 53 were infected by meat of domestic swine which had fed freely in the territory of the Caucasus Preserve—the North Caucasian Strain of *Trichinella* (NCST). In 7 cases the infection was contracted from swine which were reared in the territory of the Moscow-Oksk Preserve and in 24 cases from swine reared on meat from fur-bearing caged animals in the Karelian isthmus.

A study of the clinical-epidemiological and parasitological features of human trichinosis from ATS showed its definite differences from STS trichinosis and trichinosis caused by other strains from temperate and southern sections of the European part of the Soviet Union. For ATS trichinosis is characterized by a prolonged incubation period, relatively low muscular invasiveness (Table 1) and together with a severe course of illness marked general signs of sensitization and severe organ pathology (Table 1). The most significant difference of ATS trichinosis from trichinosis in endemic foci is the prolonged convalescent period and the frequent development of a chronic invasion phase, not a property of STS trichinosis. This phase can involve angiomyocytic cardiopathies, a chronic phenomenon of gastroduodenitis, and cerebral disturbance with psychotic reactions (Ozeretskovskaya *et al.* 1966, 1972, 1974; Ozeretskovskaya 1968).

The principal chronic course of the disease during infection with ATS appears to be an incomplete process of encapsulation of the infective organism in the muscles. In the course of the months following infection, in place of a formation characteristic of STS trichinosis, a dense fibrous capsule is observed instead of a massive kill of parasites, with violent perifocal and diffuse cellular infiltration (Fig. 1) (Ozeretskovskaya *et al.* 1966, 1969a, 1970). High titers of specific antibodies illustrate the hypersensitivity of the patients (Table 1).

The significance of the break-up of the process of encapsulation in the pathogenesis of ATS trichinosis is confirmed by the very severe course of invasion. Therapy of patients with glucocorticoids supplementarily suppress the formation of the parasite capsule (Ozeretskovskaya *et al.* 1966). There are good effects in therapy of ATS trichinosis with a specific chemical—thiabendazol (Ozeretskovskaya *et al.* 1969a, 1970; Faynfeld 1973). At the same time the specific chemical preparation thiabendazol (a derivative of benzimidazol) is less active on the muscle stage of STS trichinosis in comparison with the intestinal stage, as a consequence of the difficulty of penetration of the preparation through the fibrous capsule, and has authentically higher effectiveness in ATS trichinosis (Ozeretskovskaya *et al.* 1969a, 1970).

PARASITOLOGICAL FEATURES OF ATS

A study of ATS and its natural hosts—the polar bear and the polar fox (*Alopex lagopus*)—by Vrangl showed that there is a peculiar process of capsule formation occurring in the circulation of the parasite in its natural biocenosis (Pereverzeva and Veretennikova 1973). In contrast to the two-layered fibrous-hyaline capsules of the parasite in animals of temperate areas (Govoroz 1895; Geller 1934; Berezantsev 1960, 1962; Pereverzeva 1966), capsules of ATS trichinosis in muscles of polar bears and polar foxes have a non-typical form, multilayered with unequal hyaline regeneration of encapsulated portion of the sarcoplasm (Fig. 2a & b). An associated network of equal-dimensioned protective capsules of STS *Trichinella* and wild, temperate strains through ATS trichinosis show distinctions between hyaline layers, often obliterating vessels (Fig. 2c). Upon heating, a significant part of the larvae become non-invasive. Hyalinated cicatrices are observed in sections in place of earlier

TABLE 1. COMPARATIVE CHARACTERISTICS OF HUMAN TRICHINOSIS CAUSED BY THE SYNANTHROPIC STRAIN (STS), ARCTIC (ATS), AND SWINE PASSAGED NATIVE (PPST) OF *TRICHINELLA*.

Trichinella strain	Number of patients	Intensity of muscle invasion (larvae/g)	Incubation period	Eosiniphilia of the blood in %		Titer of serological reaction at the height of illness		Lethal outcomes
				in incubation	at height of illness	agglutination	precipitation	
ATS	18	30.5±5.9-36.0±1.4	34-200		30.0±4.54-50.0±12.3	1:32-1:128	1:256-1:1024	0 0
STS	140	17.4±2-25.5±1.7	22-600	2.93±68	22.0±4.16-33.45±3.8	1:4-1:32	1:64-1:128	0 0
PPST	84	9.2±2.1	500-22500	1.88±0.35	16.76±2.09	% negative* -1:4	% negative*	12 14.3

*SKST trichinosis

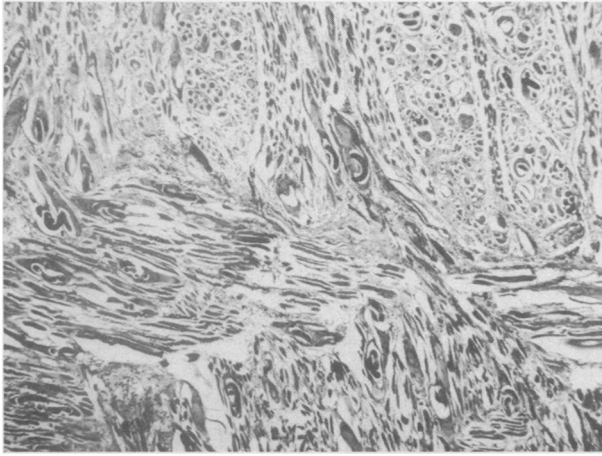


Fig. 1(a)



Fig. 1(b)



Fig. 1(c)

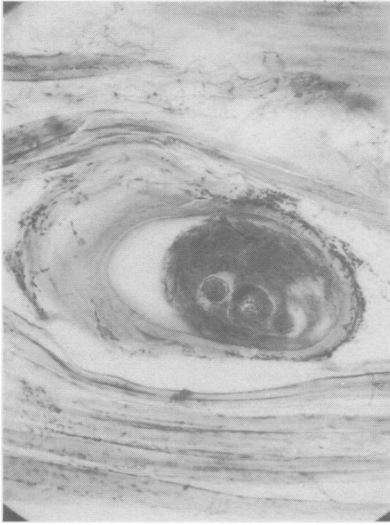


Fig. 2(a)

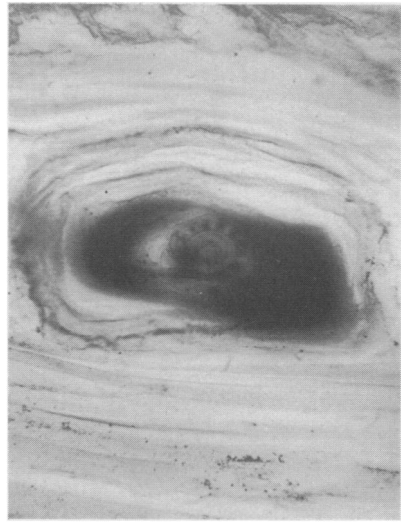


Fig. 2(b)

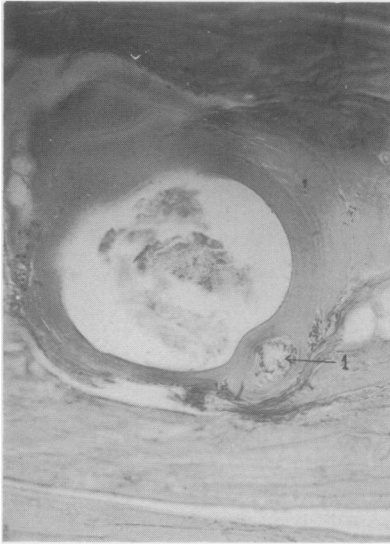


Fig. 2(c)

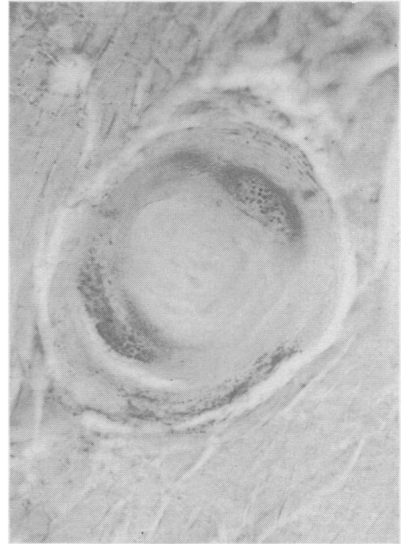


Fig. 2(d)

killed *Trichinellae* (Fig. 2(d)), not observed by us and other researchers in muscles of wild and domestic animals infected with temperate strains of *Trichinella*. Analogous peculiarities of capsule structure were discovered (Pereverzeva and Veretennikova 1973) in studies of polar bear muscles from Franz Josef Land and from arctic regions of Canada (materials of Dr. G. Dzhonkel). The capsule of ATS *Trichinella* differs morphologically from the capsule of native strain *Trichinella* found in various specimens of wild fauna of the Central European part of the Soviet Union—the wolf (*Canis lupus*), the fox (*Vulpes vulpes*), the raccoon dog (*Nyctereutes procyonoides*), etc. (Zimoroy 1963; Pereverzeva 1966).

TABLE 2. COMPARATIVE CHARACTERISTICS OF EXPERIMENTAL TRICHINOSIS IN WHITE MICE INFECTED WITH ATS, SEPST, AND LTS.

Trichinella strain	Intestinal Trichinella			Muscle Trichinella			Blood according to days after infection								
	Viability on the seventh day of invasion in % of entries	Period of* elimination from the intestine	Time of* appearance in muscles	Number in muscle	In diaphragm	Leucocytes	% Lymphocytes		% Mono-cytes						
ATS	13-15	14-15	10-12	158	2765	1611	16300	16200	8000	41	61	60	8	8	7
SEPST	15	10-12	12-13	845	1768	4080	13400	11000	6900	73	70	53	14	7	5
LTS	54	25-28	6-7	2360	10355	12281	4700	4500	16200	63	57	41	3	5	15

*Days after infection

During laboratory studies of ATS trichinosis, low association of larvae with intestinal muscles was observed and rapid disappearance of intestinal parasites (Table 2). Cellular infiltration around the intestine by *Trichinella* is significantly more powerful than during invasion by LTS and contains a higher percent of lymphoid cells. Later *Trichinella* appear in the muscles with violent cellular infiltration with predominantly lymphocytes around larvae, seeded into the skeletal muscles, disrupting the process of encapsulation and massive kill and resorption of *Trichinella* in muscle (Table 2) (Pereverzeva *et al.* 1971, 1973).

Morphological and histochemical study of muscle sections from animals invaded by ATS show slower development of parasites in comparison with LTS. Thus, in three weeks after infestation, the larvae have a cylindrical form with insufficient differentiation of internal structure (Fig. 3a), extremely insignificant content of glycogen and absence of mucopolysaccharides. Simultaneously, in LTS-infected animals by the fifteenth day a majority of larvae are already spirally twisted with organogenesis concluded; they contain a greater quantity of glycogen, acid and neutral mucopolysaccharides reflecting the active metabolism of the parasite (Fig. 3b).

Aside from the later formation of connecting capsules of ATS larvae (30-35 days instead of 20-25 days with LTS) there is undefined, absent or very weak development of a hyaline layer even 2-3 months after infection (Fig. 3c), while, with larvae of LTS, a double-layered capsule forms by the 4th week. The insufficiency of the protective function of the capsule in ATS causes a violent cellular reaction around the larva and in the interstitial tissue of the muscle, resulting in the destruction of the normal development and metabolism of parasites leading to a massive kill and lowered intensity of invasion (Fig. 3d and Table 2) (Pereverzeva 1966; Pereverzeva *et al.* 1971, 1973). Invasiveness of ATS larvae in its passaging in white mice is substantially lower in LTS infection (Ozeretskoykaya *et al.* 1969a 1971). The development of STS in laboratory animals has patterns in common with the development of ATS. However, peculiarities of the morphology and biochemistry of intestinal and muscular *Trichinella* are significantly less expressed (Table 2) (Pereverzeva 1966).

DISCUSSION

The materials presented here confirm that ATS has specific characteristics, individually defined development, and is a unique parasite with obligate and incidental hosts. It was possible to guess that features of the course of ATS-trichinosis in humans and laboratory animals are linked to its difficulty in adapting to organisms not common to the usual biocenosis of this strain. However specific the development of muscle ATS-*Trichinella* in obligate hosts, it is definitely different from *Trichinella* of the natural SEPST strain and leads to the conclusion that specific ATS can quickly be characterized by its genetic aspects.

Our clinical, epidemiological and experimental studies allow us to conclude that ATS displays genetically low immuno-suppressive activity—a property determining the possibility of one organism sharing a habit with another foreign to it in antigenic relation. In recent years we have obtained a variety of indirect and direct indicators of immuno-depressive activity of *Trichinella* (Svet-Moldavskiy *et al.* 1969, Chimishkyan *et al.* 1974). It was established that *Trichinella* separate out of the host organism low molecular weight compounds

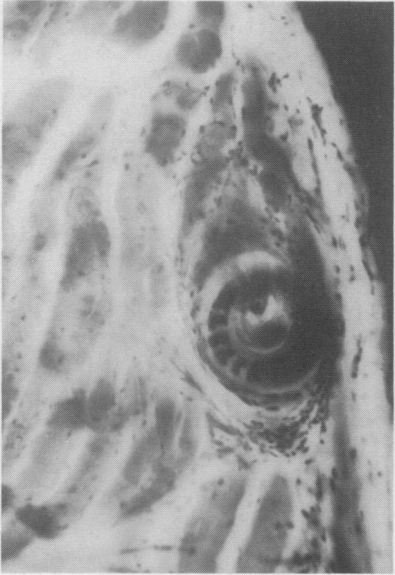


Fig. 3(b)

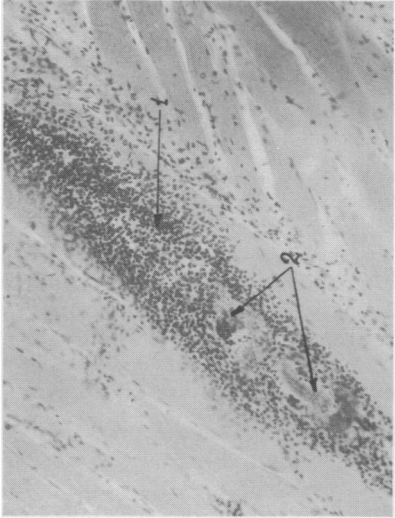


Fig. 3(d)



Fig. 3(a)

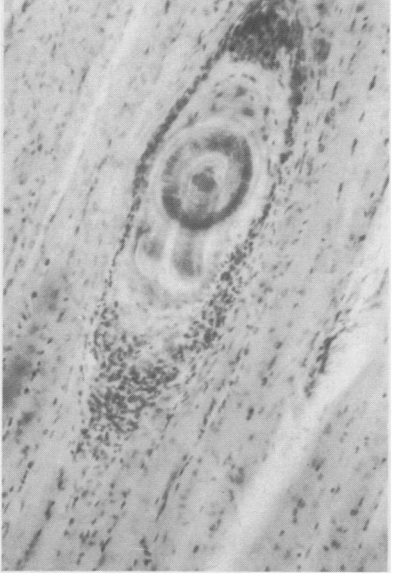


Fig. 3(c)

having the capacity for agglutinating leucocytes and producing a cytopathic effect. Analogous activity is shown by extracts of *Trichinella* from muscles (Tanner and Gaubert 1972). The immuno-depressive activity of *Trichinella* is especially pronounced 24-40 days after invasion (Chimiskyan *et al.* 1974), that is at the stage of massive encapsulation of the *Trichinella* larvae.

Low immuno-depressive activity of ATS-*Trichinella* determines the sluggish development and early evacuation of intestinal parasites, a later period of implantation of migrating larvae in the muscle, imperfections of the encapsulation and massive kill in the early period after infection on a background of active angiomyositis. The indicated biological peculiarities of the strain determine the features of the clinical course of ATS infection—prolonged incubation period, severe course of the disease (despite low intensity of invasion), and its transition to a chronic stage. The low immuno-depressive activity of ATS-*Trichinella* produces violent cellular infiltration with sharp predominance of lymphocytes around the intestinal and muscular *Trichinella* in experiments and in patients infected with ATS (Ozeretskovskaya *et al.* 1966, 1969a, 1970, 1974; Pereverzeva *et al.* 1971, 1973). Evidence of low immuno-depressive activity of ATS is shown in the uncommonly high titers of specific antibodies during the 6-12 months after infection (Ozeretskovskaya and Uspenskiy 1957; Ozeretskovskaya 1958; Ozeretskovskaya *et al.* 1974). The indicated property explains the useless effect of steroid hormones in ATS-trichinosis, the immuno-depressive effect of which facilitates the breakdown of encapsulation of larvae in the muscles and the hypersensitivity of the host organism and the shift of the disease to a chronic state (Ozeretskovskaya *et al.* 1966, 1974; Ozeretskovskaya and Tumol'skaya 1972).

Of special interest in the discussion of various immuno-depressive activity are STA and PPTS trichinosis. Favorable course of the invasive process of STS infection determines the moderate immuno-depressive activity of strains of *Trichinella* of endemic foci and the 'balanced' relationship in the host-parasite system. Under these conditions are guaranteed the quick and absolute encapsulation of larvae in muscles, securing the host from hypersensitivity and facilitating biological protection of both members of the system (Ozeretskovskaya 1968, 1970; Ozeretskovskaya *et al.* 1974). Simultaneously PPTS and especially SKTS trichinosis displays an uncommonly high immuno-depressive activity determining the malignant course of invasion and kill of the host (Ozeretskovskaya *et al.* 1969b, 1974). Together with this, SKTS is distinguished by low invasiveness in relation to laboratory rodents (Ozeretskovskaya *et al.* 1969a, 1970). Trichinosis is caused by STS and wild strains from the African continent and in *O. sumatra* also is distinguished by low invasiveness with respect to laboratory rats and also yields a lethal outcome upon infection of humans (Forrester *et al.* 1961; Nelson and Mukundi 1963; Ozeretskovskaya *et al.* 1966, 1974), thus closely resembling the characteristics of PPTS trichinosis strains in the USSR. The high immuno-depressive activity of PPTS secures rapid and complete encapsulation of larvae in muscle, despite the uncommon intensity of invasion. The complete formation of the larval capsule in the muscle despite the death of the host ensures the preservation of the parasite as a consequence of the presence of wide dietary interspecies links, cannibalism and necrophagy. Simultaneously in high arctic latitudes, with relatively scanty numbers of mammals—hosts of *Trichinella*—they are limited in consequence to the possibility of transmission and invasion through food links among them and, therefore, the *Trichinella* accumulate in the largest predators and marine mammals. The presence of aggressiveness from ATS ought to have been leading to the kill of the parasite as a species.

It is possible that the metabolic peculiarities of ATS determine features of the biochemism of muscle tissues of polar mammals. It is known that upon infection with STS and native strains, bands of *Trichinella* larvae never appear in the cardiac muscle (Merkushev 1954; Matoff and Komandarov 1965). Simultaneously we (Pereverzeva and Veretennikova 1973) found in the cardiac muscle of two out of three polar bears from Vrangal Island 0.5-1 larvae/gram of tissue.

In recent times data have been obtained that indicate that *Trichinella* selectively settle in the so-called 'tonic' muscles, rich in imidazole compounds, especially imidazole alkylamines, histamines, etc. (Ozeretskoyanskaya and Bekish 1969; Bekish 1972). Invasion by *Trichinella* is accompanied by a sharp drop of imidazoles in the skeletal muscles, also of anzerine and carnozine and a marked increase in the histamine content (Bekish 1972). It is known that natural imidazoles are connected with a high level of energy processes in the skeletal musculature (Severin 1965). It is possible to suggest that in conditions of high arctic latitudes the biochemistry of the skeletal musculature and cardiac differ from the biochemistry of muscles of mammals in temperate latitudes. Later the biochemical features of ATS may be elucidated and will explain the difficult adaptation to animals of the average spectrum and to man.

Not excluding the ATS, we distinguished two natural arctic strains—a high arctic strain from polar bears, possessing strength of ecological isolation in features of biochemistry of land mammals, the weakest immuno-depressive activity, and a strain from lower arctic latitudes from the brown bear. However, clinical-immunological features of disease and incomplete encapsulation of *Trichinella* in muscles in both cases are displayed in equal degree (Ozeretskoyanskaya *et al.* 1966, 1969b, 1974). Britov and Boyev (1972) agree to a new species *Trichinella nativa* sp. nova. ATS with other natural strains of *Trichinella*, often in synanthropic foci, in the separation of native African strains of *Trichinella* into another new species *Trichinella nelsoni* sp. nova, according to the authors not irradiating in the vicinity of man and weakly pathogenic for him, appears somewhat artificial. First of all, it is known from a series of outbreaks of human trichinosis in Africa that intensive infection of humans with lethal outcome has occurred (Forrester *et al.* 1961). Further, the morphological and functional muscle capsules of larval SEPTS strain and other native strains of *Trichinella* are similar. Finally, it is hard to explain the reasons for isolated occurrences of the African strain of *Trichinella* in the southern Ukraine, that, nevertheless, are recorded by the authors themselves.

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