

CHANGES IN ELECTRICAL EXCITABILITY AND MUSCLE RESPONSE SPEED IN DOGS WITH EXPERIMENTALLY INDUCED TUBERCULOSIS

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In our previous researches we have shown that in dogs with tuberculosis the chronaxy increases as the infection progresses, and attains a maximal value in the final stage of the disease. When the course of the disease is arrested, and clinical signs become normal, there is a gradual return of the chronaxy to its original level.

In a further study of the condition of the neuromuscular apparatus in experimental tuberculosis, we made measurements of the chronaxy and of the strength-duration curve, as well as of the lability (muscle response speed). The results are described in the present article.

METHOD

Measurements were made of the chronaxy of the flexors and extensors of the digits of the right hind feet, using a condensor chronaxiometer and Yu. M. Uflyand's standard method [4]. To determine the strength-duration curve and the muscle response speed of the gastrocnemius muscle of the right hindleg, we used an electrical stimulator made by the State Institute of Physiotherapy (1953); it was possible to regulate the intensity of the stimulus between 0 and 200 v, and its duration from 0.01 to 100 msec, the values being read off from a scale. The threshold value of the voltage for each impulse duration was plotted on special graph paper and the strength-duration curve drawn. The lability of the muscle was measured by applying pulses at rates of 1, 5, 10, 20, 50, 100, 200, 300, etc. up to 1500 impulses/second, the voltage being maintained constant at a value $1\frac{1}{2}$ times threshold, and the duration being fixed at 0.05 msec.

The contractions were recorded on a kymograph. In one experiment, 3-7 myograms were recorded to determine lability changes occurring during the course of the reaction (adoption of a "labilization" rhythm, lability constancy). We also studied the relation between the strength of the stimulus and the strength of the contraction of the gastrocnemius muscle. Using an impulse duration of 0.05 msec, and a frequency of 50 impulses/second, we measured the response to a threshold stimulus and to stimuli $1\frac{1}{2}$ and 2 times threshold. In healthy dogs the response of the neuromuscular apparatus before and after repeated lability measurements was proportional to the strength of the stimulus (see Fig. a₁). Equalization, or an abnormal stimulus response relationship which occurred after an infection, showed we were dealing with phasic conditions as described by N. E. Wedensky in his work on parabiosis [1]. To infect the dogs with tuberculosis, we used the usual laboratory method of intravenous injection of 1 mg per kg of a culture of bovine tuberculosis mycobacteria.

The chronaxy, strength-duration curve, and lability were measured before and after infection on 7 dogs — Kvartus, Kutsy, Rex, Donor, Pepper, Blacky, and Dubok. Recovery of the chronaxy, strength-duration curve, and lability were studied in 4 dogs — Kvartus, Kutsy, Donor, and Pepper, because Rex and Blacky died 50-60 days after infection and Dubok was killed by electrocution for postmortem examination.

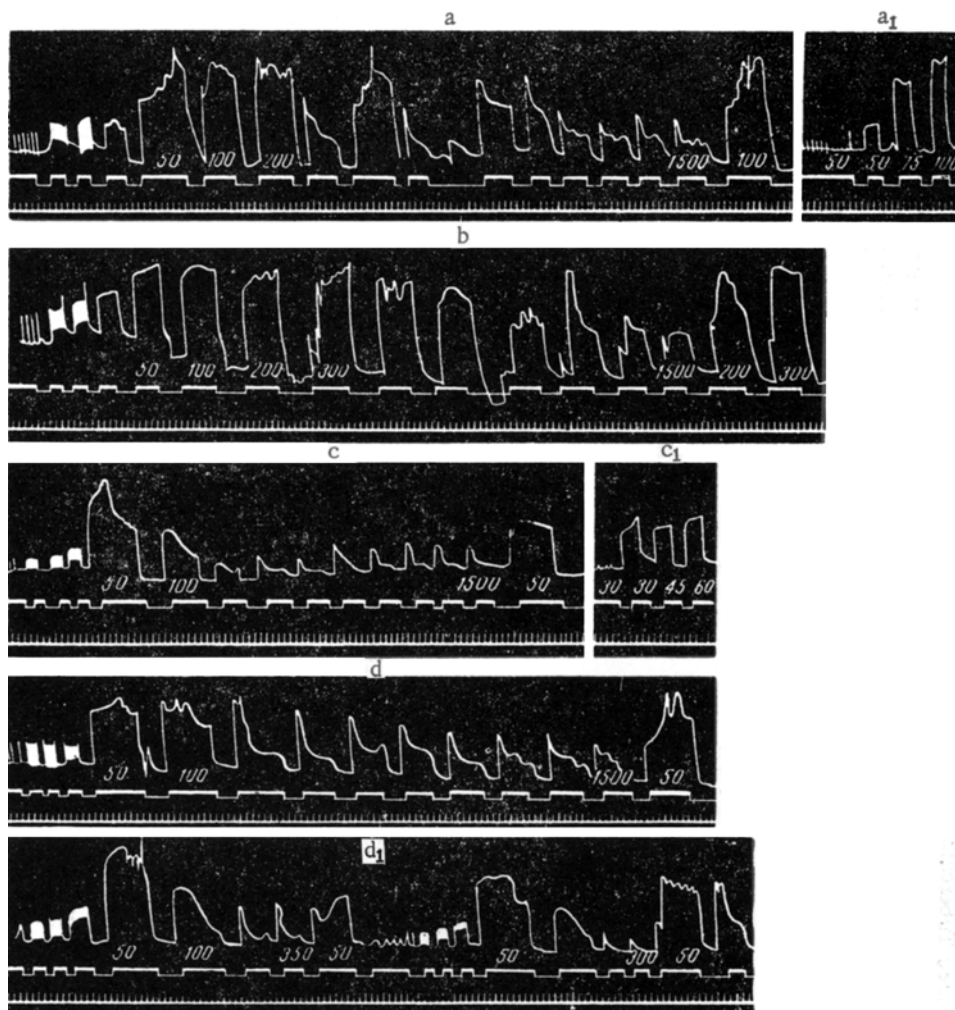


Fig. Changes in the physiological lability of the gastrocnemius muscle in experimental tuberculosis in the dog Kwartus at different times during the illness.

a) Before infection (stimulus 35 v); a₁) before infection (frequency 50 impulses/second; b) on the 7th day after infection (stimulus 15 v); c) 21 days after infection (stimulus 70 v); c₁) 21 days after infection (frequency 50 impulses/second); d - d₁) 35 days after infection (stimulus 30 v).

Curves, from above downwards: myogram; stimulus marker (frequency of impulses per second shown on myograms a, b, c, d, and d₁, and strength of stimulus in volts on myograms a₁ and c₁); time marker (1 second). Duration of impulses in all myograms 0.05 msec.

The condition of the animals which had recovered was confirmed by a positive Mantoux reaction, and in those which died the diagnosis was made from specific tuberculous changes in the lungs and pleura. On those that died - Blacky and Dukok - a test was made by culturing a portion of lung on a piece of Lowenstein's medium, when the pure culture of tuberculosis mycobacterium was grown.

We obtained 1211 myograms and 430 strength-duration curves. The condition of the dogs after infection may arbitrarily be described in terms of 4 periods: The incubational period, lasting for 4-8 days, the period of increasing clinical signs, which lasted from the 8th to the 12th day, the acute phase from the 14th to the 28th day, and recovery period (if such occurred) during the second and third months, or the terminal period if the dog died.

The first changes in the quantities measured before the manifestation of any clinical signs occurred on the 2nd-4th day after infection. The strength-duration curve was displaced towards the abscissa, and was altered in

TABLE

Changes in Physiological Lability in Dogs with Experimentally Induced Tuberculosis

Index of lability	Kvartus		Kutsy		Donor		Pepper		Dubok		Rex		Blacky	
	before infection	19 days after infection	before infection	17 days after infection	before infection	17 days after infection	before infection	19 days after infection	before infection	17 days after infection	before infection	17 days after infection	before infection	17 days after infection
Maintained tetanus	200	50	200	100	50-100	50	100	50	100	50	100	50	100	50
Decreasing tetanus	300	100	300	200	200	100	200	100	200	100	200	100	200	100
Complete pessimum	> 1500	1000	> 1500	1500	> 1500	1500	> 1500	1500	> 1500	300	> 1500	800	1000	300-400

shape, the change affecting principally its horizontal portion; this result indicated an increased excitability for both long and short stimuli. The chronaxy was shortened; it was determined by measurements made on the strength-duration curve, and had a value of 0.1 as opposed to the normal 0.16 msec; the value obtained by using a condensor chronaxiometer was 0.2 msec as against a normal value of 0.28 msec.

The physiological lability was measured in terms of the following quantities: The maximal possible frequency at which a tetanus could be maintained is known as the "frequency optimum"; the frequency at which the tetanic contraction becomes reduced is known as the "frequency pessimum"; and the critical frequency is that at which minimum contraction (complete pessimum) occurs (see Fig. a, a_1 , b, c, c_1 , d, d_1).

Before infection, in the dogs Rex, Donor, Pepper, Dubok, and Blacky, which had chronaxies of 0.36, 0.42, 0.28, 0.28, and 0.36 msec respectively, a maintained tetanus was recorded at frequencies of 50 and 100 impulses/second, while in Kvartus and Kutsy, which had shorter chronaxies of 0.24 and 0.2 msec, the corresponding frequencies were 50, 100 and 200 impulses/second (see Fig. a). In none of the dogs did a complete pessimum develop until the frequency had risen to 1500 imp/second.

In the first days after the dogs were infected, and particularly in Kvartus, Kutsy, and Blacky, lability was increased. A steady tetanic contraction occurred only at high frequencies between 200-300 per second and a decreasing tetanic contraction only at frequencies of 400-500 per second (see Fig. b). The complete pessimum at 1500 per second never occurred.

Thus, in the first days after infection and before clinical signs had appeared, excitability was increased, chronaxy was shortened, and physiological lability increased. As the disease progressed, particularly when the condition became grave, by the 3rd or 4th week, when the temperature was 41° and the erythrocyte sedimentation rate 50 mm per hour, and the animals had lost weight, the increase in excitability and lability and the shortening and variability of the chronaxy, which had occurred in the incubation period, were no longer observed, but instead there was a progressive decrease in excitability and lability, and an increase in the chronaxy.

The strength-duration curve showed two changes, one in the horizontal and the other in the vertical portion. The horizontal knee of the curve was further removed from the abscissa, i.e., even with impulses of long duration excitability was reduced. The vertical portion of the curve was removed from the ordinate, showing that even at considerable stimulus intensities a considerable stimulus duration was required.

The chronaxy as determined from the curve was 0.27-0.4 msec, and the value measured by the condenser chronaxiometer was 1.2-0.88 msec, showing an increase of 2-4 times.

In measuring physiological lability (see Table) during this period, in all the dogs a steady tetanus was recorded at a frequency as low as 50 impulses/second, though not invariably a decreasing tetanic contraction was also found at frequencies between 50 and 100 per second, while with stimulation rates between 300 and 400 per second or above, there was an initial tremor of the muscle, and complete pessimum soon developed (see Fig, c).

Measurements on the ratio of stimulus strength of muscle response showed that during this period the normal relationship was disturbed: In response to weak, average, and strong stimuli, the same abnormal effect occurred (equalizing and paradoxical phase — see Fig, c₁).

Subsequently, after treatment with 25 mg per kg phthivazide (a derivative of isonicotinic acid hydrazide), as the animals' clinical condition improved, it was found that the chronaxy was shortened. The strength-duration curves showed an increased excitability.

A more precise indication of the condition of the neuromuscular apparatus at this period is given by the lability: We determined the condition of the tissue not from the occurrence of a single contraction, but from many following closely on each other. Thus, in Kvartus, on the 35th day after infection, there was an increased lability in the first myogram (see Fig, d). The decreasing tetanic contraction was recorded at a frequency of 100-200 impulses/second. At a frequency of 1500 per second, no complete pessimum occurred. However, in subsequent myograms, the decreasing tetanic contraction occurred at frequencies as low as 50-100 per second, and a complete pessimum occurred at a frequency of 200-300 (see Fig, d₁). Before infection, no such changes were associated with repetition of the test; on the contrary, quite frequently during the reaction the excitatory rhythm was sometimes taken up, and the lability actually increased during the test. This effect indicates a failure to adapt to the rate of excitation, and a progressive decrease in lability during the test, and therefore a considerable reduction in the performance level of the nerve and muscle in question.

Compensation for and disappearance of the clinical signs occurred in the following 2-3 months, and were accompanied by a gradual return of excitability, shortening of chronaxy, and an increase in lability. At first the indices were unstable: At one time the chronaxy, electrical excitability, and lability were within normal limits, but periodically there would be an increased chronaxy, and a reduced excitability and lability. The indices appear to return to normal in two phases: At first they are variable, but at times come within normal limits, and later they remain stable at normal values. As a result of the complete restoration of function on the motor side, after 1-1½ months the animals became completely normal as judged by the usually accepted clinical signs.

It can be seen therefore, that tuberculosis involves profound neuromuscular changes which, from the way they develop, must be considered as manifestations of a parabiogenic process. This condition may result from a central nervous disturbance, from reflex effects originating in the damaged organs, or from the direct action of the tuberculosis toxin on the motor apparatus.

From our results it would appear that the chronaxy, the shape of the strength-duration curve, and the lability as measured by the optimum and pessimum frequencies of tetanic contraction, represent important criteria for the evaluation of the condition of the neuromuscular system in tuberculosis.

SUMMARY

A study was made of the condition of the neuromuscular apparatus in dogs infected with tuberculosis. Measurements were made of the chronaxy, physiological lability, and electrical excitability. The lability of the motor apparatus showed wide variations in healthy dogs before infection, and was greater the shorter the chronaxy.

Pronounced changes in the motor apparatus follow infection with tuberculosis. There is an increased excitability, a shortened chronaxy, and an increased lability during the incubation period. At the height of the disease there is a stable progressive decline of excitability, an increased chronaxy, a reduced lability, and an abnormal relation between stimulus and response; equalizing and paradoxical phases occur.

On recovery, the excitability, chronaxy, and lability return slowly to their initial values, and all clinical indices become normal.

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