

Physiology. — "*Veratrine poisoning of degenerated mammalian muscle.*"
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An investigation into the action of veratrine on degenerated muscle will give the opportunity to throw some light on two till now unsolved difficulties in the problem of the action of veratrine on skeletal muscle. The structure of muscle changes in a definite and well-known way during degeneration; if we find that veratrine has on degenerated muscle an effect different from the normal, we may be able to demonstrate a causal relation between the changed structure and the change in function. Furthermore, severance of the motor innervation is the only method possible to obtain a muscle free from nervous elements; in this way we may study the action of veratrine on striated muscle without poisoning simultaneously any nerve fibres.

As far as I know, the previous work on this subject consists of two publications only, both by FONTÈS¹⁾. He cut the sciatic nerve in frogs and poisoned after a varying interval their muscles. The contraction, obtained from the M. Gastrocnemius had the typical shape we also find in the intact muscle after veratrine poisoning.

FONTÈS made his investigation in winter; the longest interval between the section of the nerve and the poisoning of the muscle was three months. This is certainly not long enough for a frog's muscle to degenerate. I cut in some frogs the sciatic in November, and was not able to find any indication of degeneration in the muscles on the operated side in April²⁾.

Therefore it is probable that FONTÈS worked on non-degenerated muscles; the conclusions drawn by him from his experiments are not justified; I repeated the procedure, but with warm-blooded animals.

In aether narcosis under aseptic precautions I cut the N. Ischiadicus in a number of albino-mice on the left side.

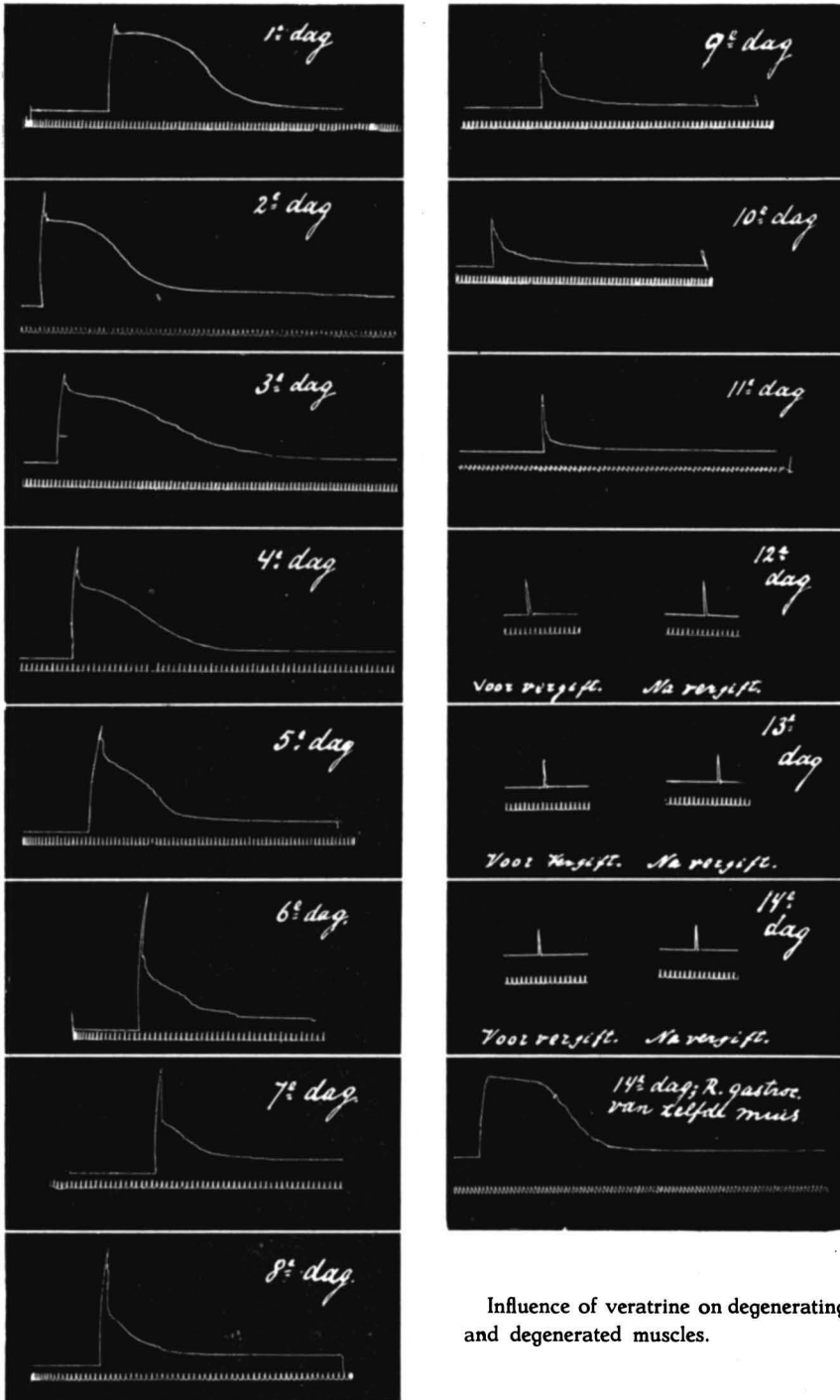
The muscles of the hind legs of those animals were tested with intervals of one day, the first 24 hours after operation.

The animals were anaesthetised with urethane (1 cc. of a 10 % solution, injected intra-peritoneally per 100 Gr. mouse). I freed the cut end of the sciatic from surrounding tissue and cut the sciatic on the other side; both tendons of Achilles were cut loose from their insertion and connected with a writing lever, providing a load of 3 Gr. The sciatic nerves were placed

¹⁾ Comptes-rendus Soc. Biol. 1921, LXVI, 84; Journ. de Physiol. et de Pathol. gén. 1925, XXIII, 292.

²⁾ Cf. BREMER and GERARD, Comptes-rendus Soc. belge de Biol. 1926, XCIV, 1035.

on a pair of stimulating electrodes; in both the Gastrocnemius muscles a pair of silver needle-electrodes were thrust. Three double-throw double-pole switches allowed a rapid change from faradic to galvanic stimulation,



Influence of veratrine on degenerating and degenerated muscles.

from direct to indirect stimulation, and made it possible to stimulate right or left without disturbing the preparation. Faradic stimuli were provided by a DUBOIS—REYMOND induction coil, the strength of stimulus being varied by changing the resistance of the primary circuit; in the table the strength of stimulus is expressed by the size of the primary current which is direct proportional to this value. In wiring the set-up care had been taken that one electrode acts as cathode on the break, both of induction shocks and of constant current; this electrode was always distal to its fellow.

When the narcotised mouse had been prepared as described above, I first compared the threshold for indirect stimuli right and left; after this the threshold for direct stimuli right and left was compared, and thereupon the behaviour of both muscles in regard to constant current.

In this way a complete insight was obtained into the stage of degeneration of the left Gastrocnemius of the tested mouse. Now I injected into both muscles 0.1 cc. veratrine solution 1 : 20,000, and compared after 3 minutes the contraction right and left on direct stimulation with induction shocks.

No clear differences are found in the first three days following the operation; after this time the differences are unmistakable. The second part of the contraction of the muscle on the operated side takes less time and is lower; small oscillations are superposed on the second part of the contraction curve. Day after day the points of difference between the contractions right and left become more distinct; the characteristic shape of the veratrine contraction disappears quite gradually in the curve from the muscle on the operated side. Twelve days after the operation we find after poisoning a contraction that is in all aspects similar to the contraction of the same muscle before poisoning. No indication of an influence of the drug can be found in the shape of the shortening curve.

We may follow the process of degeneration until the muscle has lost its direct irritability — eight weeks after section of the nerve — and during this period the effect of veratrine on the degenerated muscle does not change, and remains nil.

We observe that the first muscle that does not show any typical effect of the poisoning is the same to show a complete electrical reaction of degeneration (Vide Table). From the twelfth day following the section of the nerve the chief points of electrical degeneration are regularly present, and from this day on no difference can be found between the contraction before and after poisoning on the operated side.

Microscopic examination. BIELSCHOWSKY-preparations, made by Dr. H. C. VOORHOEVE from the tested muscles, showed, that 14 days after the section of the nerve no motor end-organs were to be found in the muscles. But in those muscles, and à fortiori in muscles that were examined at a shorter interval after operation, no difference could be detected in the structure (aspect of striation, number and distribution of nuclei, amount of sarcoplasm) compared with normal muscle.

TABLE.

Development and progress of degeneration on the operated side.

Day	Strength of current milli-Amps, used for stimulation of nerve and muscle.						
	Faradic		Galvanic				
	Nerve	Muscle	Cath. make	Anod. break	Anod. make	Cath. tetan.	Cath. break
1	0.5	0.8	2.0	3.2	5.5	10.4	22
2	0.8	1.1	1.8	3.0	4.8	12.2	22
3	0.8	1.2	2.2	3.5	5.0	12.0	20
4	1.3	1.5	2.5	4.0	4.2	12.0	21
5	1.3	1.8	2.5	3.8	4.5	10.8	18
6	2.0	1.3	2.7	4.1	4.5	10.6	18
7	2.2	2.8	3.1	5.0	4.0	12.4	19
8	3.5	3.5	3.5	5.2	4.0	11.3	22.5
9	3.4	3.7	3.8	5.4	3.8	12.0	22
10	4.6	4.0	4.0	5.5	3.8	10.5	22
11	5.7	4.0	4.5	6.0	4.1	12.2	24
12	—	4.2	6.0	7.4	5.0	11.6	22.5
13	—	4.2	5.1	9.0	4.8	8.2	18
14	—	4.5	5.4	6.8	6.0	9.4	21
15	—	6.0	5.4	7.2	4.8	10.2	15
16	—	5.5	7.0	8.5	6.2	8.5	18
17	—	6.2	7.0	8.5	5.7	7.9	17

Sympathetic. When the sciatic nerve is sectioned, of course the sympathetic innervation of the Gastrocnemic muscle is interrupted at the same time.

Therefore I performed some experiments in which the spinal innervation was left intact, and only the sympathetic nerve paths were interrupted.

In a number of rats the sympathetic chain was extirpated on the left side from the solar plexus downward.

The first of those rats was examined two weeks after the operation, the others with intervals of a fortnight after the first; the last rat twelve weeks after the operation.

Some of those animals showed a difference in temperature and in aspect of both hindlegs; one rat had a marked edema of the left hindleg and foot.

The contractions obtained from the Mm. Gastrocnemii did not show any difference before nor after poisoning between the muscles from the operated and from the intact side.

Conclusions. Muscles that are caused to degenerate by cutting their motor nerve show gradually a diminishing influence of veratrine poisoning.

From muscles that are completely degenerated as shown by electrical test, a veratrine contraction cannot be elicited; after poisoning they yield on induction shock a single muscle twitch, just as before poisoning.

This is also true for muscle that do not show any structural change when examined microscopically.

Muscles, lacking sympathetic innervation, yield veratrine contractions that are identical to those of intact muscles after poisoning.