LETTERS TO THE EDITORS

The Editors do not hold themselves responsible for opinions expressed by their correspondents. No notice is taken of anonymous communications.

Regeneration of Mammalian Striated Muscle

SINCE the classic studies of Volkmann[1] there has been abundant experimental work which shows that, following local injury, mammalian striated muscle is capable of some degree of regeneration. But this regenerative capacity is commonly held to be limited in extent and abortive so far as functional repair is concerned. It can now be stated that, under certain conditions, the regeneration of striated musculature may be much more extensive and complete.

Previous work which has been reported from this laboratory[2] showed that if the main vessels supplying the tibialis anterior muscle of a rabbit are ligatured, the lower half or two thirds of the muscle can usually be effectively devascularized and undergoes complete necrosis except for isolated fibres at the surface and alongside main anastomotic vessels, and some fibres at the lower end adjacent to the tendon. Moreover, it was found that within a few days the necrotic muscle becomes invaded by granulation tissue containing new muscle fibres of embryonic type which stream down from the ends of the surviving fibres in the upper part of the muscle.

Further experiments have now been completed in order to determine the fate of these regenerating fibres. In two rabbits, the tibialis anterior muscle of both sides was effectively devascularized. Two days later the muscles were exposed and bromophenol blue injected into the ear vein to determine the exact extent of the devascularization. In both cases the upper third of the muscle became stained in the normal manner, while approximately the lower two thirds remained unstained, with a sharp line of demarcation between the two parts of the muscle. After three weeks the muscle was resected from one side for histological examination. In each case the original muscular tissue in the lower two thirds was found to have undergone practically complete dissolution, and to be replaced in great part by strands of newly formed fibres extending down from above. The muscle of the other side was removed after three or four months. In one case it was somewhat shrunken and showed histologically patches of fibrosis and fatty infiltration in the lower two thirds, but there was also a considerable amount of mature muscular tissue. In the other case the muscle appeared quite normal to superficial inspection, and was found histologically to be composed of muscular tissue of approximately normal mature structure. It thus appears that in the rabbit the lower half or two thirds of the tibialis anterior can become completely reconstituted after undergoing ischæmic necrosis.

These experiments have provided abundant material for the study of the histogenesis of regenerating striated muscle, and this is now being undertaken. It may be said, however, that the material provides no support for the contention of Levander (recently expounded in *Nature* and elsewhere[3,4]) that in the course of the regeneration of mammalian muscle new muscle elements arise by the differentiation of generalized connective tissue cells; on the contrary, they appear to be formed entirely as outgrowths of pre-existing muscle fibres, thus confirming the conclusions of many other students of muscle regeneration.

Levander's conclusions seem to be based on an erroneous interpretation of the histological picture. In our material we have frequently seen the appearance of isolated 'myoblasts' arranged, as he describes, like a shoal of fish in the granulation tissue. But if these are examined by serial sections, the appearance is found in all cases to be due to the oblique sectioning of long continuous strands which can be ultimately traced without interruption to the stumps of pre-existing fibres. If there has been much distortion of the tissues (as has evidently occurred in Levander's material, in which necrosis was induced by the intramuscular injection of alcohol), the connexion between the young fibres and pre-existing fibres may not be easy to establish without the detailed study of large numbers of serial sections. Levander also supports his interpretation by the appearance of young muscle fibres in the neighbourhood of pieces of muscle transplanted into the subcutaneous tissue. He assumes that the original fibres of the transplant undergo complete necrosis. In fact, we have found that in such transplants some of the muscle fibres at the surface may survive and retain their vitality. Moreover, it should be noted that the outgrowth of new muscle fibres from old fibres proceeds with great rapidity. Their maximum rate of growth is at least 1 mm. a day.

Thus *individual* sections may show newly formed fibres at some distance from the position of pre-existing fibres, suggesting an independent origin. Our experiments do not, of course, exclude the possibility of such an origin, but this can only be established by experiments of a more critical character.

W. E. LE GROS CLARK.

Department of Anatomy,
University, Oxford.
June 11.

[1] Volkmann, R., *Beitr. path. Anat.*, **12**, 233 (1893).
[2] Clark, W. E. Le Gros, and Blomfield, L. B., *J. Anat.*, **79**, 15 (1945).
[3] Levander, G., *Arch. f. Klin. Chir.*, **202**, 677 (1941).
[4] Levander, G., *Nature*, **155**, 148 (1945).

Motor Response from Giant Fibres in the Earthworm

IT has recently been shown[1,2,3] by action potential records from the giant fibres that these form two systems; the two laterals are interconnected and act in unison independently of the median. Since the discharge from either fibre system may produce the sudden end-to-end shortening of the worm, the question arises why the nerve pathway is double. Stough's answer[4,5] that the median giant will only conduct backwards and the laterals forwards is incorrect, for their action potentials can be shown normally to run both ways[1,3].

A new fact emerges, however, for the sensory field of the median giant is found to be mainly from the first forty segments, and for the laterals from the remainder of the worm (at least in the conditions of the experiments). So it is natural to look for a difference in the two motor responses adapted to escape from attack at the head or at the tail respectively. This is the case.

If the worm is on a slippery surface, the giant fibre response when either head or tail is touched is a shortening towards the middle because (from mech-