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Failure of the Gas Gangrene Organism to Proliferate Within Nerve Bundles.

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In the course of a study of experimental gas gangrene in guinea pigs, the relative resistance of nerves to invasion by *Cl. welchii* was frequently noted. The literature on the histopathology of gas gangrene of the peripheral nervous system gives few details of conditions within nerves. In one case of human gas gangrene from which we obtained postmortem material, however, examination of microscopic sections of the groin musculature showed a single *Cl. welchii* lying between axis cylinder and myelin sheath. This nerve was contained within an edematous nerve bundle and the latter was in the midst of a necrotic area. This one observed instance of an organism in this position so emphasized the usual absence of these organisms from very close proximity to nerve fibers in both experimental infection in guinea pigs and natural infection in man, that an attempt was made to induce growth and proliferation of the organisms by depositing them directly within the nerve bundles.

The growth* from 5 cc of the supernatant of a 24-hour chopped meat culture of *Cl. welchii* (strain WX) was suspended in 1 cc of 10% $CaCl_2$. Of this suspension, 0.1 cc was injected directly into the sciatic nerve of the guinea pig on one side in 6 animals. The needle, 27 gauge, was directed proximally. It penetrated the nerve about 2 cm distal to the sciatic notch and was pushed forward into the nerve for a distance of about 0.5 cm. The object was to deposit the organisms either within the nerve bundle or very close to a nerve bundle. This succeeded in most cases and was checked by following the rupture of epineurium and perineurium caused by the needle, and also by occasionally finding the organisms between nerve fiber and myelin sheath at the place of injection. In the latter cases, judged by their staining reaction the organisms were always dead before the nerve was fixed. There was never clear evidence of proliferation of the organisms at this site.

After 40 hours, the animals were sacrificed and the sciatic nerve

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examined. Conduction distally through the nerve was almost nonexistent in most cases. The nerve was then excised from the sciatic notch to a few millimeters beyond the point of insertion of the needle, fixed in 10% formalin, sectioned in paraffin and stained by Goodpasture's modification of the Gram method. The vertebral canal was opened, the spinal cord examined, and in some cases the latter was also prepared by the above method. Examination of sciatic nerve sections never revealed active organisms lying within the myelin sheaths of nerves or between sheaths. The connective tissue sheaths outside the nerve bundles, however, invariably showed large numbers of organisms in active proliferation in both proximal and distal directions. Although devoid of organisms, nerve fibers, myelin sheaths and adjacent connective tissue showed varying degrees of edema. Animals permitted to die of the infection frequently showed extreme necrosis of these tissues. Only after the nervous tissue had been reduced to a pulpy mass, the original nature of which was only just recognizable, were the organisms found invading the debris.

In one case the infection was found to have invaded the vertebral canal, but microscopic sections of the distal portion of the cord and its coverings showed the nervous tissue to be free of organisms while the meninges were freely attacked. This infection had undoubtedly travelled through the connective tissue and epineurium by way of the sciatic notch, and entered the vertebral canal through vertebral foramina. Nowhere along this pathway were the organisms detected within nerve bundles, but were found in profusion in adjacent epineurium and connective tissue. The same result was also obtained by depositing the organisms within the connective tissue around the sciatic notch.

Even in loosely organized tissue the effects of the gas gangrene toxin are usually recognizable well in advance of its actual invasion by the organisms. Apparently, the less dense the tissue or organ the more rapid is its invasion by this organism; the pronounced tendency of gas gangrene to proliferate along fascial planes is well known. It is suggested that in the case of the peripheral nerves the epineurium and surrounding areolar connective tissue offer a more favorable mechanical, and possibly physiological, base for growth and proliferation of the organism and thus successfully delay nerve invasion until the immediately available connective tissues of the region have been destroyed.