

mentary or alternative. It may be that in this phenomenon of cancer susceptibility there may be still another influence, whose nature is not yet determined, that is also

involved in the origin of tumors. Some geneticists believe that this may be in the form of a somatic mutation.

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Influence of Spinal Section on Tissue Permeability.*

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The experiments reported here were designed to determine the effect on tissue permeability of transections of the spinal cord at levels varying from the first to the fifth thoracic segment. The spreading of india ink suspensions in the cutaneous connective tissue was used as indicating the degree of connective tissue permeability. Tissue permeability measured in this way is affected by constitutional, nutritional and functional conditions and by the spreading factors (Duran-Reynals)¹ but no influence of the nervous system has been demonstrated. McClean's² results, obtained in excised skin, were interpreted as indicating that spreading is independent of vasomotor or other nervous stimuli.

The present study was designed to determine whether or not the nervous system is involved in the regulation of tissue permeability in living animals.

Materials and Methods. Twelve animals (11 rabbits and 1 dog) were used as follows:

India ink with saline and india ink with spreading factor[†] were injected into the skin of the upper and lower part of one side of the animal's body. Twenty-four hours later the extent of spread of the ink spots was recorded by drawing the areas on cellophane and measuring their surfaces in square centimeters with a planimeter.

The spinal cord was then completely transected under local anesthesia at levels varying from the first to the fifth thoracic segment.

Following operation injections of identical amounts of the same mixtures of india ink and saline and of india ink and spreading factor were repeated on the opposite side of the animal's body, care being taken to select injection sites comparable to those used before operation. This was repeated after 24 hours and every subsequent day until all available skin surface was used (usually 3 to 7 days). Twenty-four hours after injection the spread of india ink was traced and measured in the manner indicated above.

For purposes of control 3 animals were laminectomized without spinal cord injury and treated similarly.

All animals were kept in a warm box at 35°C after operation to prevent loss of body heat. Repeated blood pressure readings were taken before and after operation. In all instances the central ear artery was utilized and the blood pressure as determined by oscillometric methods showed constant variations ranging between 65 mm Hg and 95 mm Hg before and after operation.

The spinal animals developed paralysis of the hind legs, urinary bladder and rectal sphincter and in several instances ataxia of

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¹ Duran-Reynals, F., *Bacteriological Reviews*, 1942, **4**, 197.

² McClean, D., *J. Path. Bact.*, 1931, **34**, 459.

[†] India ink (Higgins) was used, diluted in equal parts of saline. All injections contained 0.25 cc of this suspension. The saline injections contained in addition 0.5 cc of physiological NaCl solution. The injections of spreading factor contained 0.5 cc of leech extract in saline 1:10 or extract of rats' testicles in saline 1:10 (0.5 cc). This material was supplied by Dr. Duran-Reynals whose help and advice are deeply appreciated.

the front legs was noted. The latter rabbits were unable to feed and for this reason, food was withheld from the controls. In other respects, the animals remained in good condition throughout the experiment.

Results. Marked reduction of the spread of india ink was observed in the skin of all spinal animals and occurred in areas above as well as below the level of section of the spinal cord. The reduction in spread was evident in the first sample, injected immediately after operation, and became more pronounced in subsequent injections. After laminectomy, control animals showed either no change or a slight increase in the size of the intradermal ink spots. Chart I presents the results observed in 3 spinal animals (rabbits 8, 9 and 10) and in the control animals (rabbits 14, 15 and 16).

The spread of india ink was reduced in skin areas injected with spreading factor as well as in regions treated with saline. The

same proportion in the amount of spread that characterized these substances in intact animals persisted after operation. Pertinent data appear in Chart II in which the columns represent the average amount of spread 24 hours after injection. This was calculated by dividing the total extent of spread in all animals by the number of injection sites.

The activity of the spreading factor can be expressed by the figure obtained by dividing the extent of spread observed in areas injected with the factor by the amount of spread in control areas injected with saline. In the present experiments these values were 1.31 before operation, 1.14 in the first 24 hours following operation, 1.37 in the second 24 hours, 1.26 in the third 24 hours, 1.43 in the fourth 24 hours and 1.25 in the fifth 24 hours. It is clear that the relative activity of the spreading factor was not affected by spinal section.

Comments. The facts presented indicate

CHART - I

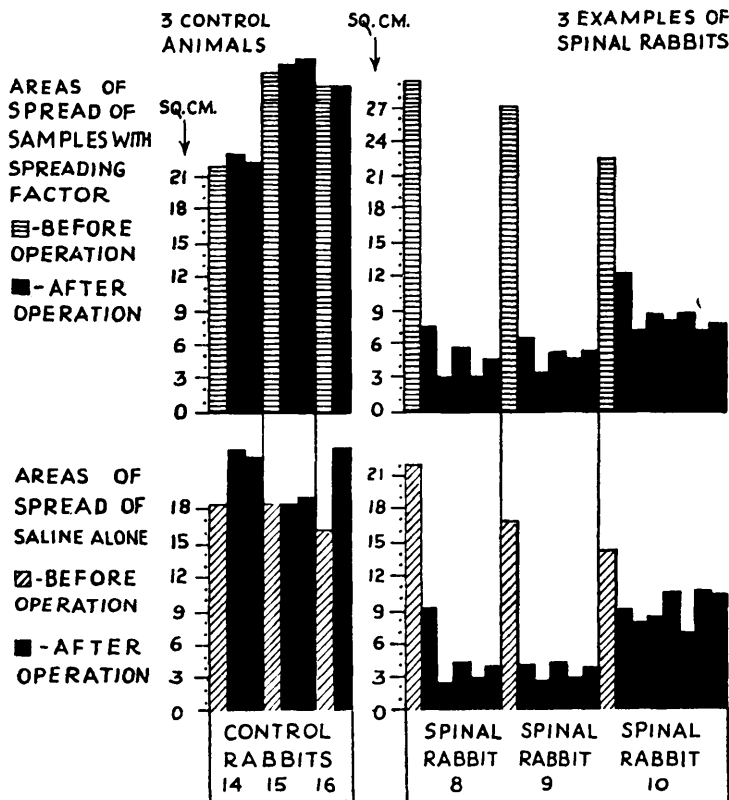
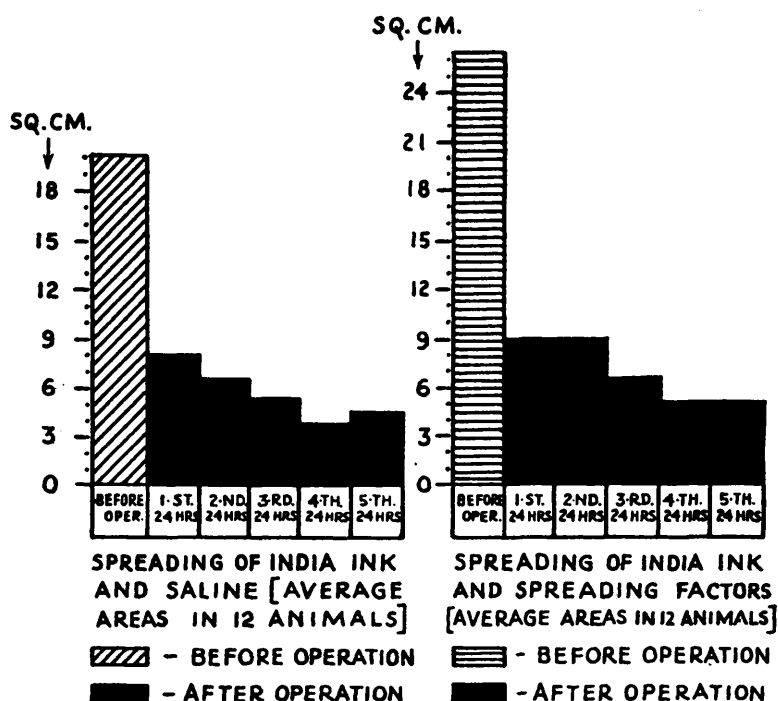


CHART-II.

that the nervous system takes part in the regulation of connective tissue permeability. The changes observed cannot be due to simple denervation as they occurred above as well as below the level of spinal section. The diminished connective tissue permeability cannot be referred to changes in blood pressure as, contrary to the observations of Wilson and Rigdon,³ pressure alterations in these experiments were insignificant. It should be emphasized that the observations of these authors³ applied to the permeability of the capillary endothelium rather than to the permeability of connective tissue and the dis-

crepancies between their results and those presented here illustrate the fact that the permeabilities of these tissues are not identical.¹ The general reduction of permeability following spinal section is in agreement with the work of Lauer⁴ who found diminished inflammatory reactions in spinal rabbits above as well as below the spinal section.

Summary of Results. Transection of the spinal cord results in a reduction of connective tissue permeability. The reduction occurs above as well as below the site of spinal section. The reduction is not dependent upon an altered activity of the spreading factor or upon the trauma of operation.

³ Wilson, H., and Rigdon, R. H., *Arch. Surg.*, 1942, 45, 416.

⁴ Lauer, N., *J. Med. de l'Ukraine*, 1939, 9, 37.