

following intravenous injection of 30 mg. of methylene blue per kilo body weight.

Each of 5 dogs which received methylene blue (in quantities ranging from 15 to 40 mg. per kilo body weight) developed an anemia the severity of which was greatest with the larger doses. In 2 experiments, otherwise less complete than that reported, the oxyhemoglobin ( $O_2$  capacity) of the blood was determined on the first and second days following methylene blue injection and was found to be only slightly below the preinjection level, although several days later it had fallen to severely anemic levels. This fact and the absence of hemoglobinuria and hematuria during the entire period following dye injection indicate that there is no immediate massive destruction of cells in the circulation.

Experiments designed to relate quantitatively dosage to response and to determine the mechanism of the methylene blue action are in progress. We also have in mind the possibility that methylene blue may find practical application in the treatment of polycythemia vera.

## 7397 P

### Conduction of Cortical Impulses to the Autonomic System.

W. C. HUNSICKER, JR., AND E. A. SPIEGEL.

*From the Department of Experimental Neurology, D. J. McCarthy Foundation, Temple University School of Medicine, Philadelphia.*

Clinical as well as experimental observations show that the cortical centers of vegetative organs are, in many instances, in close topical relation to those of adjacent skeletal muscles. The descending cortico-fugal tracts to the peripheral part of the autonomic system are topographically related to the pyramidal tract. They also lose their excitability after destruction of the motor cortex and frontal lobe, within the same time as do the corticofugal somatic fibers. (Spiegel,<sup>1</sup> Friedberg.<sup>2</sup>) It seemed, therefore, of interest to ascertain whether the pyramidal tracts by themselves can conduct cortico-fugal impulses to the autonomic system. The experiments were performed on 30 cats. In a first series, the "extrapyramidal" fibers that arise from the hypothalamus were severed by deep incision into

<sup>1</sup> Spiegel, E. A., *Zentren. des autonomen Nervensystems*. Berlin, Springer, 1928. *Bull. Johns Hopkins Hosp.*, 1932, **50**, 237.

<sup>2</sup> Friedberg, Ch., *Z. ges. Neurol.*, 1931, **50**, 134.

the floor of the 4th ventricle. The central grey matter and tegmentum in the pons and midbrain were destroyed where the centrifugal fibers of the hypothalamus are located. In a second series of experiments, the conduction of cortical impulses to vegetative organs was studied after transverse section of both pyramidal tracts on the base of the pons. After the lesion of either of these systems had been performed, the effects of stimulation of the motor cortex and the frontal lobe was noticed on the pupil, the blood vessels, the heart, the sweat glands and the urinary bladder.

In the study of the *pupil*, the lesion of the brain stem was combined with unilateral cervical sympathectomy. Thus, cortical stimulation elicited on the pupil ipsi-lateral to the sympathectomy only inhibition of the sphincter, on the other pupil inhibition of the oculomotor plus stimulation of the sympathetic.

Severance of the systems arising from the hypothalamus produced a myosis and prolapse of the nictitating membrane that in some cats was not at all, and in others but slightly changed after cervical sympathectomy. Section of the pyramidal tracts was not followed by myosis. In stimulation of the cortex the dilatation of the pupil with intact cervical sympathetic was more pronounced when the pyramidal tracts were severed than when the hypothalamic pathways were cut. At times maximal dilatation of the pupil was observed in cortical stimulation despite pyramidal destruction. In other words, the pyramidal tract has no such tonic influence upon the spinal segmental centers of the cervical sympathetic as has the hypothalamus, the pupillodilatator centrifugal cortical impulses use the hypothalamic systems to a larger extent than the cortico-spinal neurones.

The *blood pressure* was recorded before as well as after curare paralysis was produced. After curarization vaso-constrictor reactions were more rarely observed in cortical stimulation than vasodilator reactions. These reactions were present in both series of experiments, but were somewhat better preserved when only the pyramidal tracts were severed than after section of the fibers dorsally to the peduncles.

In some experiments, the *electrocardiogram* was recorded. Only a relatively small change of the heart-rate (slight tachycardia as well as slight bradycardia or both reactions following each other) were brought about. Such changes were observed in stimulation of the frontal lobe with the brain stem intact as well as after both types of lesions.

A similar result was obtained in studying the activity of the

*sweat glands* under cortical influence by recording the galvanic skin response. The reaction observed after both types of lesions of the brain stem was as a rule weaker than with the brain stem intact, particularly after severance of the hypothalamic tracts.

On the *bladder*, cortical stimulation produced stimulating as well as inhibitory effects. It is interesting to note that not only the stimulating, but also the inhibitory reactions depend mainly upon the pelvic nerves. The increase of bladder activity as well as the inhibition of this organ were observed in both series of experiments. The severance of the extra-pyramidal tracts did not impair these reactions to a greater extent than did the section of the pyramidal tracts.

It is concluded that there exists a double (pyramidal and extra-pyramidal) conduction of cortico-fugal impulses to the autonomic centers in the cord.

## 7398 P

Mechanism of Invasiveness in the Genus *Streptococcus*.

E. W. DENNIS AND D. A. BERBERIAN. (Introduced by G. H. Miller.)

*From the Department of Bacteriology and Parasitology, American University of Beirut.*

Menkin<sup>1</sup> recently demonstrated that various materials are fixed *in situ* when injected into an acutely inflamed area, and that the mechanism of fixation of such substances as bacteria and trypan blue is primarily mechanical obstruction in the form of a fibrinous net-work and thrombosed lymphatics at the site of inflammation. Obviously the speed with which an inflammatory irritant causes the region to be blocked off is a significant factor in determining its ability to disseminate into the contiguous tissues or blood stream. Menkin<sup>1</sup> observed that *Staphylococcus aureus* caused the formation of thrombi in the lymphatics and fixation of trypan blue within about one hour after their introduction into the skin of rabbits, while the more invasive *Streptococcus hemolyticus* produced fixation only about 45 hours later. Menkin believed that the delayed fixation in the latter case was due to the "relatively mild local effects" of the streptococcus.

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<sup>1</sup> Menkin, V., *J. Exp. Med.*, 1933, **57**, 977.