ERYTHROCYTOSIS OR SYMPTOMATIC POLCYTHEMIA FOLLOWING CHRONIC CEREBRAL STIMULATION THROUGH INDWELLING ELECTRODES*

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(Received for publication October 1, 1959)

In preliminary studies to assay the effects of repeated long-term stimulation of cerebral autonomic centers, pentylentetrazol (Metrazol) given intravenously or intramuscularly evoked predominantly generalized vasopressor responses in cats and one of the most consistent concomitants of this repeated vasopressor response in the cat was hypertrophy and hyperplasia of the pulmonary arteries. In these chronic experiments, examination of the blood showed a notable increase in count of the red blood cells, and it was speculated that this condition might resemble the clinical entity of Ayerza’s disease (pulmonary arteriosclerosis with polycythemia).

A review of the literature reveals several reports of experiments on laboratory animals in which an erythrocytosis or reticulocytosis resulted from direct physical stimulation of the brain or ablation of cerebral areas. Schulhof and Matthies injected sterile siliceous earth in the region of the hypothalamus of rabbits to cause a sterile inflammatory reaction simulating an encephalitis. Three of their animals showed an increase in count of the red blood cells of 1 to 2 million. Dockhorn produced a reticulocytosis in human subjects by the application of diathermy to the brain stem. Mettler found a reticulocytosis of 0.3 to 7.4 per cent in dogs following bilateral frontal lobectomies and no such response was seen after a bilateral occipital lobectomy.

There is a wide range of normal counts of red blood cells in cats and dogs. Trautmann and Fiebiger gave values of 7.2 ± 1 million cells per c.mm. for the cat and 6.1 ± 1 million cells per mm. for the dog. A major cause of polycythemia in animals is exposure to high altitude, and the degree of polycythemia depends upon the severity of hypoxia and the duration of the exposure. It is of particular interest to the present study that this type of polycythemia disappears after cervical transection of the spinal cord.

The present experiments were undertaken to determine, first, whether the medial hypertrophy and hyperplasia of cats’ pulmonary arteries, pre-

* Presented at the meeting of the Harvey Cushing Society, New Orleans, Louisiana, April 30, 1950. This investigation was supported by research grants (Nonr-1134(02)) from the Office of Naval Research, Department of the Navy and (B-1759) from the National Institutes of Health, Public Health Service.
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viously reported, were associated with an erythrocytosis; secondly, it was desired to establish whether the arterial vascular changes and the erythrocytosis could be produced by chronic focal electrical stimulation of cerebral autonomic centers through indwelling electrodes. This was pertinent since electrical stimulation has been used so extensively as a means of eliciting responses from both the human and animal brain.

**EXPERIMENTAL METHODS**

These investigations were conducted on 9 adult male and female dogs (4 years or younger in apparent age) and 14 adult male and female cats.

**METHOD OF STIMULATION**

(1) **Control Studies.** To determine whether the operative procedures and insertion of electrodes caused any peripheral-blood response, 1 adult cat and 1 adult dog were studied hematologically for a period of over 1 year after implantation of the electrode without stimulation. The remaining 13 cats were examined for an average of 1 month and the remaining 8 dogs for an average of 4 months before operation and/or stimulation.

(2) **Pentylenetetrazol Studies.** A series of 6 adult male and female cats were given a subconvulsive amount of pentylenetetrazol (30 mg.) intramuscularly 4 times daily for 4 to 6 weeks. The blood for counts was obtained from the ear every other day. The blood for hematocrits was drawn once a week from the femoral vein.

(3) **Indwelling Electrode Studies.** In a group of 9 dogs and 8 cats, 27-gauge stainless-steel wire electrodes, insulated with polytetrafluoroethylene (Teflon), were inserted aseptically through small trephine openings and oriented, manually or stereotaxically, in cortical loci of the prefrontal and pyriform areas. For this procedure the animals were anesthetized with 2.5 per cent thiamylal sodium (Surital Sodium) given intravenously. The electrodes were fixed in position by a stainless-steel holder (described by Sheatz) bolted to the skull. Postoperatively, the cats received 600,000 units of aqueous procaine-penicillin, intramuscularly, daily for 1 week and the dogs received 600,000 units of aqueous procaine-penicillin and 1 gm. of streptomycin daily for 1 week.

All electrical stimulation was carried out without anesthesia and was delivered from a sine-wave phase-shift oscillator driving a cathode follower output (60 c./sec.; 0.2–4.0 volts). Eight dogs were stimulated in a pattern of 10 min. every hour, 6 times a day, 5 days a week. Stimulation was started 2 weeks postoperatively and was continued for a period ranging from 3 to 6 months. In the series of 7 electrically stimulated cats, 2 animals received 10-sec. stimulations every 2 min. for about 6 hours a day; 2 cats received 30-sec. stimulations every 5 min. for about 6 hours a day; and 3 cats received 10-min. stimulations every hour for about 6 hours a day. The cats were stimulated for periods of 1 to 6 months.

**BLOOD AND HISTOLOGICAL STUDIES**

Both the control and indwelling-electrode groups of animals were weighed twice a week. A blood-volume determination (T-1824 [Evans] blue dye technique) and the hematocrit were done at least once a week. Total count of red blood cells and white

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