Hypothermia has been used effectively to protect tissues from irreversible damage caused by circulatory arrest, whether the latter is of accidental occurrence or induced in the course of an operative procedure. Relatively little attention, however, has been given to the possibility of providing such protection by chemical means. Chemical protection against ischemia might be expected to be more easily and quickly induced than hypothermia and to be free of some of the undesirable cardiovascular side effects of the hypothermic state. Three classes of potential protective agents can be envisaged: (1) agents designed to maintain the patency of the vasculature during the ischemia in order to insure complete perfusion of the tissue following its termination; (2) inhibitors of cellular activity that would lower the metabolic demands of the tissue during the ischemia; (3) physiological compounds, added in excess of their normal concentrations, to forestall the first irreversible changes in the cells. Beneficial effects from pretreating ischemic kidneys with heparin and studies demonstrating extension of the period of permissible cardiac standstill with compounds producing cardioplegia have suggested the feasibility of the first two approaches. Surprisingly little systematic study has been devoted to the third possibility.

Controlled study of cerebral ischemia and of factors modifying its effects has been hampered by the unavailability of suitable experimental preparations. Production of temporary but total arrest of circulation to the brain is difficult to achieve in commonly available laboratory animals because of the large vertebral-anterior spinal artery axis and the abundant muscular collateral vessels which communicate with the carotid system. Previously described methods have had the undesirable features of damage to the spinal cord, impairment of circulation to other organs, or problems of recovery from thoracotomy.

In the experiments described below, a relatively simple operative technique has been developed and tested for producing temporary cerebral ischemia in cats. This technique has been used to determine possible effects of several substances on the period of ischemia that can be reversibly sustained. The substances tested included two barbiturates, ethyl alcohol and solutes added to the blood to increase its osmolarity.

Methods

**Technique for Producing Temporary Cerebral Ischemia.** The procedure developed involved occlusion, by means of an initial operative technique, of all arterial inflow to the brain except that provided by the common carotid arteries. The animal then was allowed to recover. At the time of the experiment it was anesthetized again, this time very lightly, and both common carotid arteries were exposed and occluded temporarily with rubber-shod clamps.

In preliminary studies to identify the collateral circulation to the cat's brain, Micropaque® barium sulfate was injected into the left auricle with the basilar and both common carotid arteries occluded. The chief collaterals were found to be: (a) the superior thyroid arteries which anastomose with branches of the inferior thyroid; and (b) branches of a large muscular artery which arise laterally from the common carotid near the level of the superior thyroid artery and communicate with divisions of the thyrocervical trunk and ex-

Received for publication October 7, 1963.

* This investigation was supported by research grants from the National Institute of Mental Health (MH-K3-3768) and from the National Institute of Neurological Diseases and Blindness (NB-04512).

* Made by Damancy and Co., Ltd., Ware, Herts., England. The size of the particle is between 0.5 and 3μ.
ternal carotid arteries (Fig. 1). The ramifications of these muscular vessels are largely in the posterior cervical region. The relative paucity of these arterial collaterals in the cat led to its selection, rather than the dog, for these studies.

At a first-stage procedure, using sterile precautions, the basilar artery, the superior thyroids and the ascending and descending branches of the large muscular arteries were occluded (Fig. 2). The technique for occlusion of the basilar artery was similar to that used in dogs by White and Donald. A longitudinal incision, approximately 4 cm. in length, was made just to the right of the thyroid cartilage and trachea. The fascial plane between trachea and carotid sheath was developed by blunt dissection; and, after placing a 15 gauge needle in the distal portion of the trachea, a self-retaining retractor was inserted to displace the trachea and esophagus to the left. This metal cannula was used to prevent suffocation from the necessarily forceful retraction of the trachea. The longus capitis muscle was detached from its origin at the base of the skull to expose the ventral rim of the foramen magnum. The dura mater was separated gently from the foramen magnum with a dental spatula, and a craniectomy was performed extending rostrally approximately 8 by 12 mm. between the tympanic bullae. The dura mater was opened in a cruciate manner with careful avoidance of the circular sinus just inferior to the foramen magnum. A segment of basilar artery free of branches was selected caudal to the posterior inferior cerebellar arteries (which in the cat arise from the basilar instead of the vertebral arteries). This was mobilized gently with fine forceps and occluded with a metal clip (Fig. 3). A small piece of gelatin foam was placed over the dural opening and the wounds were closed with interrupted sutures of 4-0 black silk.

In this preparation no bone is removed from the convexity of the skull, and since the tentorium of cats is bony it seems unlikely that the small amount of bone removed over the ventral aspect of the medulla provided any significant decompression for the brain. It was not possible, however, to obtain a watertight closure of the small incision in the meninges at the site of craniectomy, so some drainage of cerebrospinal fluid into the soft tissues of the neck presumably occurred.

Each animal received penicillin, 300,000 units, by intramuscular injection at this initial procedure. The mortality for this first-stage operation was approximately 10 per cent. Anisocoria was frequent in the surviving animals, which otherwise seemed intact neurologically.

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**Fig. 1.** Angiogram of head and neck of cat made by injecting Micropaque into the left auricle after the basilar artery and both common carotid arteries had been occluded. Note that the contrast agent fills the distal carotid circulation by entering chiefly through the large muscular branch.

**Fig. 2.** Sites of arterial occlusion in the cat whereby the brain is made dependent for its blood supply on both common carotid arteries. CCA = common carotid artery. MB = muscular branches. STA = superior thyroid artery. ICA = internal carotid artery. PA = pharyngeal artery. AB = anastomotic branch. IMA = internal maxillary artery. ACA = anterior cerebral artery. MCA = middle cerebral artery. PCA = posterior cerebral artery. PICA = posterior inferior cerebellar artery. VA = vertebral artery. ASA = anterior spinal artery.