

there is a threshold concentration, not achieved in the central portion of compact chromatolytic cell groups, which must be reached before the virus can become destructive. Heretofore an immunity of the cells of the CNS has been achieved only in the presence of active poliomyelitis virus. The real importance of these experiments lies in their demonstration of the fact that resistance to destruction by virus may be evoked in the normal cell without antecedent exposure to the infective agent.

## 10903

**Surgical Production of Collateral Intracranial Circulation.  
An Experimental Study.**

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Beck<sup>1, 2, 3</sup> and O'Shaughnessy<sup>4, 5, 6</sup> have demonstrated that an effective collateral blood supply to the heart can be established by the use of pedicled muscle and omental grafts. Others<sup>7, 8, 9</sup> have similarly employed the omentum to augment the circulation to the kidneys. The present experiments<sup>10</sup> were performed to determine whether an accessory arterial blood supply from an extracranial source could be provided for the brain by applying to its cortical surface a pedicled graft of temporal or suboccipital muscles.

Monkeys (*Macaca mulatta*) weighing 2 to 3 kilos were used as experimental animals. The operative approach and technic, as well as the sequence of the procedures, varied slightly during the course of

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<sup>1</sup> Beck, C. S., *Ann. Surg.*, 1935, **102**, 81.

<sup>2</sup> Beck, C. S., and Tichy, V. L., *Am. Heart J.*, 1935, **10**, 849.

<sup>3</sup> Mautz, F. R., and Beck, C. S., *J. Thoracic Surg.*, 1937, **7**, 113.

<sup>4</sup> O'Shaughnessy, L., *Brit. J. Surg.*, 1936, **23**, 665.

<sup>5</sup> O'Shaughnessy, L., *Lancet*, 1937, **1**, 185.

<sup>6</sup> O'Shaughnessy, L., Slome, D., and Watson, F., *Lancet*, 1939, **1**, 617.

<sup>7</sup> Davis, H. A., and Tullis, I. F., Jr., *PROC. SOC. EXP. BIOL. AND MED.*, 1939, **40**, 161.

<sup>8</sup> MacNider, W. deB., and Donnelly, G. L., *PROC. SOC. EXP. BIOL. AND MED.*, 1939, **40**, 271.

<sup>9</sup> Mansfield, J. S., Weeks, D. M., Steiner, A., and Victor, J., *PROC. SOC. EXP. BIOL. AND MED.*, 1939, **40**, 709.

<sup>10</sup> German, W. J., and Taffel, M., *Proc. Third Internat. Neurol. Congress, Copenhagen, Denmark, 1939*, in press.

the experiments, but the main objectives in each instance remained the same. After either preliminary or concomitant ligation of one or more of the main arteries to the brain, the superior border of the temporal muscle was separated from its origin and reflected to expose most of the underlying squamous portion of the temporal bone. The muscle was left attached at its insertion and its blood and nerve supply not disturbed. A large defect was made in the temporal bone, the exposed dura excised, and the underlying arachnoid peeled gently away from the cerebral convolutions. The periosteal surface of the temporal muscle was scarified and applied directly to the denuded brain. The superior border of the muscle was sutured to the remaining free edge of the dura at the margin of the bony defect. No sutures were placed between the muscle and the brain itself. In 2 of the animals pedicled grafts of the suboccipital muscles were placed over the cerebellar hemispheres in addition to the bilateral temporal grafts. At varying intervals the animals died or were sacrificed and the accessory circulation was studied by arterial injection methods, by specimens cleared according to the Spalteholz technic, and by histological sections.

I. The first group of experiments was designed to test the functional efficiency of the artificially produced collateral blood supply. The serial ligations of the 4 major arteries were all performed in the neck.

a. Monkey No. 8.

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|---------------|--|
| Oct. 11, 1938 | Ligation of left internal carotid artery.  |
| " 12          | Left temporal muscle graft applied.  |
| Nov. 8        | Ligation of right vertebral artery.  |
| " 9           | Right temporal muscle graft applied.   |
| Dec. 6        | Partial ligation of right internal carotid artery. Some difficulty with breathing noted during operation, but animal made complete recovery. |
| " 20          | Complete ligation of right internal carotid artery. Respirations irregular and labored. Death.   |

At autopsy both vertebral arteries were ligated in the neck and India ink injected into each common carotid artery. All the larger arteries of the brain were later found to contain the ink. The muscle grafts (6 and 9 weeks old) were firmly adherent to the surface of the brain. Histological studies revealed these grafts to be joined to the brain by a loose vascular fibroblastic layer which was infiltrated throughout with a moderate number of mononuclear cells and occasional polymorphonuclear leukocytes. The cellular infiltration extended deeply into the muscle graft but was inconspicuous in the underlying cerebral cortex. In serial sections, large and small thin-walled blood vessels were seen to course from the muscle through the inflammatory connecting zone where they communicated with surface

pial vessels, or directly with the cortical vessels emerging from the substance of the brain. India ink particles were visualized in most of the arteries of the brain, the muscle, and the connecting zone.

b. Monkey No. 72.

- Dec. 7, 1938 Ligation of left internal carotid artery; left temporal muscle graft.  
 Jan. 4, 1939 Ligation of right vertebral artery; right temporal muscle graft.  
 Feb. 1 Partial ligation of right internal carotid artery.  
 " 15 Complete ligation of right internal carotid artery.  
 Mar. 1 Partial ligation of left vertebral artery.  
 " 16 Complete ligation of left vertebral artery.  
 Apr. 4 Animal sacrificed. The monkey suffered no obvious ill effects from any of the operative procedures.

Autopsy: The calvarium was rongeuired away and silver clips applied intracranially to both vertebral and both internal carotid arteries. A 1% aqueous solution of trypan blue was then injected slowly, first into one common carotid artery and then the other. The dye was seen to course slowly through the temporal muscle, cross over directly from the muscle into the large pial vessels and then spread in a fan-like fashion over the surface of the brain. After the injection of about 15 cc, some of the dye passed upwards through the vessels on the medial wall of the cerebral hemisphere to meet the circulation of the dye coming directly over the convex surface of the brain. This seemed to indicate the passage of the dye from the muscle graft through intermediary vessels to the circle of Willis, and thence to the anterior cerebral arteries. All the above phenomena were observed on both sides.

When the brain was removed the arteries and arterioles everywhere were stained with the dye. The muscle grafts were solidly fused and well stained. The vascular connections between the muscle and the brain were demonstrated in thin sections cleared by the Spalteholz method.

On microscopic examination the connecting zone on the right side (12-week-old graft) was composed of a layer of fibroblasts rich in blood vessels. The cellular infiltration was present but slight. Between the connecting zone and the muscle there was a layer of dense pink staining fibrous connective tissue which communicated frequently with the fibrous sheaths between the muscle fasciculi. This layer, with wavy and irregular surfaces, appeared to be the regenerated deep temporal fascia and periosteum which had been scarified prior to the application of the graft. The histological picture on the left side (16-week-old graft) was essentially the same except that the fibroblasts in the intermediate zone were more mature, more closely packed, and began to resemble adult connective tissue cells.

c. Monkey No. 9. Control.\*

- Oct. 19, 1938 Ligation of left internal carotid artery.

Nov. 16	Ligation of right vertebral artery.
Dec. 14	Partial ligation of right internal carotid artery.
" 28	Complete ligation of right internal carotid artery.
Jan. 11, 1939	Partial ligation of left vertebral artery.
" 25	Complete ligation of left vertebral artery.

The animal continued to thrive despite the fact that the 4 major vessels had been ligated. No muscular weakness or paralyses were noted.

March 22, 1939. Thorotrast was injected into common carotid arteries and an effort made to visualize the natural anastomotic channels radiographically. This was not successful. Animal sacrificed.

Definite collateral vascular channels joining the brain and the adherent temporal muscle have been demonstrated both in the histological sections and by the injection technic. Inasmuch as the ligation of both internal carotid and both vertebral arteries was well tolerated by the control animals, no definite conclusions can be drawn from these experiments concerning the efficiency of the accessory extracranial vascular communications.

II. In an effort to exclude as much as possible the naturally existing collateral arterial channels proximal to the circle of Willis, the arterial occlusions were performed intracranially. Two of the major vessels were clipped at operation, and the remaining 2 at autopsy immediately prior to the injection with the dye. In animals No. 73 and No. 90 the procedure was varied by preliminary ligation of these vessels in the neck and by the application of suboccipital muscle grafts to the cerebellum. In these latter 2 animals the internal carotid arteries were at no time obstructed intracranially.

a. Monkey No. 73.

Dec. 7, 1938	Ligation of left internal carotid artery.
Jan. 4, 1939	Ligation of right vertebral artery.
Feb. 1	Partial ligation of right internal carotid artery.
" 15	Complete ligation of right internal carotid artery.
Mar. 1	Partial ligation of left vertebral artery.
" 16	Complete ligation of left vertebral artery.
" 29	Left temporal muscle graft applied.
" 31	Right temporal muscle graft applied.
May 10	Both vertebral arteries occluded intracranially with silver clips; bilateral suboccipital muscle grafts applied to cerebellum. All of the above procedures were well tolerated.
June 23	Animal sacrificed. Common carotid arteries injected with India ink and gelatin mixture.

At autopsy the arterioles in the brain were well outlined with the India ink. The temporal and suboccipital grafts were firmly adherent to the cerebral and cerebellar hemispheres respectively.

Cleared thin sections demonstrated abundant vascular communicating channels between the brain and all the muscle grafts.

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\* In addition, animals No. 73 and No. 90 served as controls for this experiment during the period from December to May (protocols below).

## b. Monkey No. 90.

In this animal the serial operations as well as the time intervals between them were in all respects identical with those of monkey No. 73. Postmortem examination revealed the arterioles of the brain to be filled with the ink and gelatin mixture. The temporal and suboccipital muscle grafts were firmly adherent.

## c. Monkey No. 57.

Apr. 27, 1939 Right internal carotid artery occluded intracranially with silver clip; right temporal muscle graft applied.

May 17 Left internal carotid artery occluded intracranially with silver clip; left temporal muscle graft applied. Following this operation the animal became unresponsive, and appeared as though decerebrate. There was a complete paralysis of the third cranial nerve on the left side. Death occurred on May 19, 1939.

At autopsy the calvarium was rongeuired away, and silver clips applied intracranially to both vertebral arteries. A trypan blue solution was injected into each common carotid artery. On the right side (3-week-old graft) the dye was seen to pass readily from the temporal muscle to the brain exactly as described in animal No. 72. On the left side (2-day-old graft) none of the dye crossed from the left temporal muscle directly to the brain. Eventually the left half of the brain was stained with dye which had come from the right side. On cross section the dye was again concentrated chiefly in the right side. The right temporal graft was firmly adherent to the brain. The left was attached only loosely by delicate fibrinous adhesions.

*Results.* An accessory and abundant arterial blood supply for the brain was experimentally produced in monkeys by the use of pedicled temporal and suboccipital muscle grafts. The newly formed connecting channels between the muscles and the brain have been demonstrated to be patent as early as 3 weeks after the application of the graft. Inasmuch as the cervical ligation of both internal carotid and both vertebral arteries was well tolerated by the control animals, no definite conclusions can be drawn from these experiments concerning the functional efficiency of these new vascular communications.

The grafts were solidly attached to the underlying brain by a vascular layer of fibroblasts which gradually assumed the characteristics of adult connective tissue cells.

The clinical application of this method for supplementing intracranial circulation should be preceded by further experimental observations including long-term studies, which are now in progress. Cerebral arteriosclerosis, recurrent cerebral thromboses, and intracranial aneurisms requiring internal carotid ligation suggest themselves as possible examples where augmentation of the intracranial circulation would be desirable.