Cerebral Circulation and Perfusion in Experimental Increased Intracranial Pressure*

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To study the pathological changes in different areas of the brain of cats subjected to increased intracranial pressure, the animals were perfused with glutaraldehyde to ensure in situ fixation of the tissue for light- and electronmicroscopy. Intracardiac perfusion of the glutaraldehyde gave excellent fixation of the brain in five cats studied as controls. However, in one animal when a marked increase of intracranial pressure was produced by inflation of an extradural balloon, the glutaraldehyde barely reached brain tissue and merely filled some of the large cortical vessels. A second experiment revealed identical findings except that the cerebellum was partially fixed. Since the perfusion material was injected at the terminal stage when the compressing balloon had been evacuated and intracranial pressure had returned to zero following a marked elevation, the finding appeared to have considerable significance.

To explore the cause of this failure of perfusion, further experiments were done and different dyes were used. In some animals the cerebral circulation was also observed through a cranial window, to compare the results with those of perfusion.

Technique

The technique of insertion of the extradural balloon and the monitoring of the vital signs has already been described in the preceding paper (see pp. 16–20). The glutaraldehyde was perfused essentially with the same technique as that described by Palay, et al., for osmium tetroxide, and by Rewcastle for glutaraldehyde. The chest was incised in the midline and the pericardium opened. The descending aorta was clamped just above the diaphragm and a large cannula inserted into the left ventricle. The right ventricle was then opened, and 1000 ml of 5% glutaraldehyde in cacodylate buffer were injected in 30 minutes. The glutaraldehyde flask was encompassed by ice chips in a bottle held 5 feet above the animal.

In addition to perfusion with glutaraldehyde, in 40 cats we used Evans blue, barium sulfate, and India ink in smaller amounts; 50 ml (60% suspension of barium, or 2 ml/kg of Evans blue or India ink) were injected into the left ventricle. In all animals the right ventricles were opened for free drainage of the venous blood. The technique of perfusion was identical for the controls and for the animals with cerebral compression.

Tracheostomy was performed at the beginning of all experiments. Initially, artificial respiration was used when the chest was opened for perfusion. As experience was gained, the time required to open the chest and initiate perfusion was shortened to 15 or 30 sec, and artificial respiration became unnecessary.

In 15 animals an additional burr hole was made just behind the recording balloon, and a circular area of the dura was removed. A glass window made to fit the burr hole was inserted in the opening and fixed in place by a plastic washer, sealed to the skull with dental cement. The cortical vessels were observed through an operating microscope, using magnification of 25 to 100. Photographs and motion pictures were taken through the microscope. These animals were also perfused at the end of the experiment, and the results of observations through the windows were compared with the results of perfusion.

In each animal the perfusion was done at a different stage during the rise of intracrara-
nial pressure, so that a clinical correlation could also be made. Following the perfusion, the brains were immediately removed, photographed, and sectioned for histological studies.

Results

**Perfusion in Normal Animals Without Cerebral Compression.** Perfusion was carried out in ten control animals without cerebral compression (glutaraldehyde in five animals, Evans blue in two, India ink in two, and barium sulfate in one). The brains were well perfused; the cortex of the cerebrum and cerebellum, the central gray matter, and the nuclei were denser in color than the white matter, appearing as dark yellow, dark blue (Figs. 1 A and 2 A), and bluish black respectively. The brains were fixed well with glutaraldehyde similar to brains fixed for weeks in formalin. The vessels were stained with Evans blue and with India ink, but Evans blue penetrated the brain slightly better, probably because it combined with plasma albumin. Although the vessels were fixed with glutaraldehyde they could not be seen well because of their light yellow color. The cortex of the brain of one animal in which barium sulfate was perfused appeared white, but the deep and fine capillaries were not perfused, presumably because of the size of the barium particles.

**Cerebral Perfusion at Different Stages of Cerebral Compression and Increased Intracranial Pressure.** Animals perfused at different stages of the rising intracranial pressure were divided into five groups. (In Groups 4 and 5 the perfusion was done after deflation of the balloon to study the cerebral perfusion following cerebral decompression.)

**Group 1.** In 10 animals the balloon was inflated gradually until the arterial and intracranial pressures rose to the highest peak and then gradually declined. The perfusion was performed when the intracranial pressure had returned to about zero. When respiration stopped and the arterial pulse was barely present, the chest was opened and the intracardiac perfusion was done. However, the perfusion substances did not reach the brain tissue (Figs. 1 B and 2 B). The vessels were either filled with clotted blood or empty. Frequently, the larger vessels were perfused but the dye did not fill the capillaries (Figs. 1 C and Fig. 4). Sometimes cerebellum was partially perfused (Fig. 1 D).

In these animals, as in the controls, the pericranial and facial muscle, the eyes, the tongues, and mucous membranes were well fixed or stained with Evans blue or India ink. But unlike the control animals, the brains were not perfused.

**Group 2.** In five animals the perfusion was done when one or both pupils were enlarged but before the blood pressure became elevated or as it was just beginning to rise. At this stage the respiration and the pulse rates were decreased. The slow waves and lower amplitude in the EEG were present on the ipsilateral side, and to a lesser degree on the contralateral side. In these animals the larger vessels were stained but capillary perfusion was markedly decreased (Fig. 2 C).

**Group 3.** In two animals the brain was perfused when the respiration began to change. The amount of Evans blue reaching the brains was more than the previous groups but not adequate (Fig. 2 D).

**Group 4.** In five animals the balloon was inflated until both pupils were dilated, the EEG was flat, and the intracranial and arterial pressures were at their peak or declining. Then the balloon was deflated. The intracranial pressure returned to zero or near it. Four animals died within 30 minutes. One animal whose respiration was artifically supported for 15 minutes died 5 hours later; during these five hours the intracranial and arterial pressure were normal but the electroencephalograms were almost flat. It is of utmost interest that, in spite of deflation of the balloons, the perfusion material did not reach the brains in this group in which the brains were almost identical with those in the first group (Fig. 3 A).

**Group 5.** In three animals the balloons were deflated before the marked rise of the arterial pressure and complete dilatation of the pupils occurred. Perfusion of the brain was then decreased. Better staining, however, was obtained if the brain was not perfused immediately after deflation of the balloon. Figure 3 B shows the