Red Venous Blood: Occurrence and Significance in Ischemic and Nonischemic Cerebral Cortex*

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The occurrence of bright-red blood (rather than blue or bluish-red blood) in surface veins of the cerebral cortex of man and animals is a striking phenomenon, although it may be overlooked by an unsuspecting or inattentive observer. Red venous blood (R VB) has been seen flowing from normal or abnormal cerebral tissue in a number of situations. Abnormal vessels that pass arterial blood directly into venous channels, such as the shunts that occur in arteriovenous malformations and tumors, frequently are associated with bright-red venous blood.8 RVB has been seen during and after seizures, whether spontaneous or induced by electrical stimulation11 or chemical stimulation.12 When cerebral ischemia is relieved, as after the release of a temporary clamp from a cerebral artery in animal studies or during surgery for aneurysms in humans, generalized or focal RVB may develop16 (Feindel, W., unpublished observations; Sundt, T. M., Jr., unpublished observations). Generalized reddening of cerebral venous blood may occur after the restoration of flow of adequately oxygenated blood following cardiac arrest or after clamping the great vessels or the trachea.11

RVB has been noted in human cerebral cortex in veins draining cystic or scarred areas,2,11 presumably related to earlier cerebral infarction. In addition, RVB has been seen in animals in regions of brain made ischemic by occlusion of a middle cerebral artery.19 Systemic hypoglycemia, produced by injecting insulin, may cause RVB to develop in ischemic cortex of animals.10 Because of the implication that venous oxygen saturation is greater than usual, the occurrence of bright-red blood in veins draining ischemic tissue is surprising. In this paper, data about red cerebral venous blood will be presented, and theories about the development of RVB in ischemic cerebral tissue will be reviewed.

Methods

Data from studies of 128 cats and 38 squirrel monkeys have been analyzed. Fifty-four cats were anesthetized with halothane; pentobarbital was used in the other 112 animals. The right middle cerebral artery (MCA) of each animal was exposed by the extradural approach14 and occluded with a clamp or clip. The surface of the cerebral cortex was exposed bilaterally by craniectomy, and protected with a thin covering of plastic (Saran). The superficial cortical microvasculature was observed through an operative microscope and photographed.19

In the 54 cats anesthetized with halothane, regional cortical blood flow (CBF) was measured by digital analysis of the appearance and disappearance at the cortex of the radioactivity of krypton-85 injected in the brachiocephalic artery.17 Mean systemic arterial blood pressure (MABP) was monitored in each animal with a strain gauge or manometer attached to a catheter placed in the femoral artery. Spontaneous fluctuations of MABP occurred in many animals; additionally, in 24 cats with CBF measurements, MABP was changed by the intravenous injection of phenylephrine (Neo-Synephrine) or sodium nitroprusside.17 Arterial carbon dioxide tension (PaCO2), arterial oxygen tension (PaO2), and arterial pH were measured in the 54 cats with CBF measurements. Thirty of these (those that did not have MABP changed) were curarized and ventilated mechanically, and PaCO2 was changed by altering the amount of CO2 in the inspired air. Hemodilution was studied in 22 squirrel monkeys and seven cats by the intravenous injection of concentrated salt-poor human albumin, low-molecular-weight dextran, 5% dextrose, or physiologic saline solution.15 Observations and measure-
ments were made from minutes to days after MCA occlusion, and at varying levels of MABP and $\text{Pa}_\text{CO}_2$.

**Results**

**Nons ischemic Cortex.** Nearly anything that was done to the exposed (but otherwise normal) cerebral cortex of the animals could lead to the development of RVB. Removal of the dura after craniectomy in both the cats and the squirrel monkeys was followed by transient reddening of the blood in surface veins approximately three fifths of the time (14 of 23 times in a series of animals in which RVB had been noted as present or absent). After removal of the dura, RVB was generalized, but lasted a few minutes at most.

Undue retraction or pressure on the cerebral cortex, or inadvertent laceration or damage from cautery, could produce RVB that was generalized or focal in the area of damage. Subdural, subarachnoid, or intracerebral hemorrhage, air embolization, and other similar occurrences were often followed by the development of RVB. None of these invariably produced RVB; whether a given situation would be followed by reddening of venous blood was unpredictable.

Red venous blood did not develop spontaneously in the superficial veins of the nonischemic cerebral cortex of any animal if respiration, blood pressure, and other systemic factors were relatively normal. Likewise, a change of MABP did not produce RVB in any animal. Correspondingly, CBF of nonischemic cortex did not change appreciably with changes of MABP.

When the $\text{Pa}_\text{CO}_2$ was increased, the superficial arterial vessels of the cortex dilated and the CBF increased. In a series of 20 cats, when an increase of $\text{Pa}_\text{CO}_2$ produced a CBF of more than 2.0 ml/gm/min (total of 19 measurements), blood in surface veins invariably was bright red (Fig. 1). When CBF was less than 1.0 ml/gm/min, blood in surface veins invariably was blue (total of 41 CBF measurements). When CBF was between 1.0 and 2.0 ml/gm/min, RVB was uncommon (seen 30 times in a total of 99 measurements). RVB was seen at CBF rates as low as 1.13 ml/gm/min, but not until CBF was more than 1.7 ml/gm/min did the incidence of RVB exceed that of blue venous blood (Fig. 1). When RVB developed in response to an increase of $\text{Pa}_\text{CO}_2$, it was present in all visible cerebral veins (Fig. 2).

**Ischemic Cortex.** After the cerebral cortex of the animals was made ischemic by the occlusion of a middle cerebral artery, RVB could develop within minutes (Fig. 3), or be noted after removal of the dura several days later. RVB that developed spontaneously in an ischemic cortex could be generalized, throughout all visible veins, but more frequently it occurred in only one venous branch or one venous tree. If focal, RVB in one branch of a vein was seen to flow into a larger vein, side by side with blue venous blood from another area of the cortex (Fig. 3). Laminar flow of differently colored blood has also been observed in association with tumors and seizures.

RVB occurring focally in association with ischemia of cortical tissue usually was present in regions where other ischemic changes were developing, or near the periphery of areas of severe ischemia. If RVB was present in areas of cortex that had severe ischemic changes, then it was present also in other surface veins, including veins draining areas of less severe ischemia.

When RVB appeared spontaneously in ischemic cortex, it could be transient, lasting only a few minutes, or could persist to the termination of the experiment as long as 5 hours later. However, once RVB disappeared and blood in the veins reverted to a bluish color, there rarely was a spontaneous recurrence of reddening.

CBF was measured bilaterally 18 times in 10 animals that had RVB develop spontaneously in ischemic cortex. Three of these 18 times RVB was associated with blood flow rates higher than those of the hemisphere opposite the occluded MCA. The other 15 times, however, RVB was present despite CBF rates lower than those of the opposite hemisphere; in two instances RVB was seen when CBF was between 0.20 and 0.30 ml/gm/min.

As with nonischemic cortical tissue, local trauma, surgical damage, or air embolization often was followed by the development of RVB. Similarly, RVB could be produced in ischemic cortex initially, or for a second time in an area in which RVB had been noted previously, by alteration of systemic or local factors. Increasing the MABP produced focal or