Editorial Views

The Humpty Dumpty Phenomenon

“When I use a word,” Humpty Dumpty said, in rather a scornful tone, “it means just what I choose it to mean—neither more nor less.”

“The question is,” said Alice, “whether you can make words mean so many different things.”

“The question is,” said Humpty Dumpty, “which is to be master—that’s all.”

Alice was too much puzzled to say anything; . . .

We, the Humpty Dumptys of the cerebral blood flow laboratories, have confounded the Alices of the clinic. We have befuddled them with words—intracerebral steal, the Robin Hood syndrome, luxury perfusion, rCBF—and their response has been a justifiable state of confusion. Consider the choice of anesthetic technique for carotid vascular surgery when the vessel must be temporarily occluded. Today nearly every conceivable anesthetic technique is being touted as the logical one. The gamut is run from hypercarbia and hypertension with cyclopropane, through hypercarbia with nitrous oxide or halothane, to hypothermia with hyper-, normo-, or hypocarbia. It is necessary now to clarify both our thoughts and our terminology, and to attempt to reach agreement on the basic facts and the logical conclusions.

At the root of our present thinking on localized cerebral vascular problems is the phenomenon of vasomotor paralysis. Blood vessels in and near an ischemic area of brain are subjected to hypoxia, hypercarbia, and acidosis—all potent stimuli for vasodilatation. These vessels are probably maximally dilated. The overwhelming dilatory stimuli in their local milieu override other factors. The vessels are thus unlikely to constrict when hypocarbia is induced by hyperventilation or to dilate further when hypercarbia is produced by carbon dioxide inhalation. They will not constrict as normal vessels do in the face of hypertension and, of course, cannot dilate further, as normal vessels do, when hypotension occurs. They have lost the property of autoregulation. Regional cerebral blood flow (rCBF) through some of these vessels at the periphery of injured areas may be extraordinarily high when blood pressure is elevated. Even when blood pressure is normal, some of these maximally dilated vessels can carry high rCBF, producing the syndrome of luxury perfusion. The rCBF then exceeds regional cerebral metabolic requirements (rCMR).

New factors are introduced when adjacent normal areas of brain are considered along with the region of vasomotor paralysis. Hypercarbia dilates normal cerebral vessels, and rCBF increases in normal areas, at the expense of rCBF in areas where vasomotor paralysis exists. This is the intracerebral steal. Some have attempted to reverse it. They have tried to produce constriction of normal vessels in order to divert flow to vessels in ischemic areas. When this can be done with hypocarbia, an inverse cerebral steal, or Robin Hood syndrome, is present.

Do these interesting situations occur in patients? Yes! Can we guess which syndrome will occur in whom? No! We cannot reliably predict how a diseased area of brain in a given
patient will respond to high or low carbon dioxide tensions, or blood pressure alterations. We cannot foretell the outcome because the anatomy and pathologic physiology are a little bit different in each patient. The variability is illustrated in this issue of the journal in the paper "The Effects of CO₂ and Systemic Hypertension on Cerebral Perfusion Pressure during Carotid Endarterectomy," presented by Fureade and his associates. These authors studied anesthetized patients whose carotid arteries were occluded during endarterectomy. They utilized pressure in the distal end of the occluded internal carotid (stump pressure) as an estimate of anastomotic flow from unoccluded cerebral vessels. In six patients stump pressures were highest when $P_{aCO_2}$'s were low; but in three other patients stump pressures were greatest when $P_{aCO_2}$'s were elevated. Two of these three "different" responses were attributed to increased systemic arterial blood pressure with hypercarbia. But again, systemic blood pressure increased with hypercarbia only in some patients, but not in others. The variability among patients with the same disease speaks for itself.

The reader of this paper will find in it illustrations of many of the phenomena of regional flow. Loss of autoregulation is demonstrated in the variation of stump pressure with arterial blood pressure, in three patients (fig. 4). Complete vasmotor paralysis is demonstrated by patient 1a (table 1), whose stump pressure did not change with either elevated or decreased $P_{aCO_2}$. Luxury perfusion is demonstrated by the very high mean "CBF equivalent." CBF equivalent is essentially the reciprocal of the arteriovenous difference in oxygen content. When the oxygen consumption rate ($\text{CMR}_O_2$) is constant, the CBF equivalent is proportional to CBF. Of course, in patients with cerebral vascular disease, rCMR may change with increase or decrease in rCBF; and CBF equivalent is not then a good estimator of flow. However, it does reflect the ratio of blood flow to oxygen consumption. Its value is normally 15 ml blood/ml O₂, and during hypercarbia it might be expected to increase to 25 ml blood/ml O₂. The value of 50 ml blood/ml O₂ during hypercarbia in these studies must be regarded as luxury perfusion.

In other parts of this paper, the reader may find illustrated the intracerebral steal (Patient 7, table 1) and the Robin Hood syndrome (Patients 2, 4a, 4b, 6 and 7, table 1). In no patient in this study was there evidence of a significant decrease in flow to the occluded side when $P_{aCO_2}$ was lowered. This phenomenon, however, has been reported in a patient who evidenced decreased rCBF in the distribution of an occluded middle cerebral artery when hyperventilation was attempted. In that case the Robin Hood syndrome went awry, and one wonders why the clinical picture has not received its rightful name—The Sheriff of Nottingham phenomenon.

Let us accept the basic phenomena, the picturesque names, and the variability among patients. We must then ask—what is a practical clinical approach to the patient with regional cerebral vascular problems? We hope that those who treat such problems will soon be equipped to measure rCBF, and will do so before, during, and after a proposed therapy or anesthetic. If rCBF is measured in four, eight, or 16 areas of a hemisphere, and if changes are observed when $P_{aCO_2}$ or blood pressure is increased or decreased, rational and effective treatment can be provided. The equipment and technology for these measurements are available today. The know-how and the means of paying for their use must be developed.

The final question becomes, "What is the anesthetic technique of choice for carotid vascular surgery? What are we to do until rCBF can be measured during anesthesia and operation?" An educated guess as to what kind of treatment fits each patient can be attempted, but this is not a completely satisfactory solution. Decrease in metabolic requirements seems to be a more rational approach, which could provide additional protection to hypoxic or underperfused cerebral tissue, whatever the anatomic or physiologic lesions might be. Reliance upon general anesthetics as metabolic depressants is unwise, as the degree of depression of CMR$_O_2$ is not great, even at significant depth. Furthermore, what is depressed appears to be only the metabolism associated with consciousness, or mental activity. What is desired is depression of metabolic needs associated with mental activity, and of those associated with maintenance of tissue integrity.
Dimensions of Anesthetic Uptake

Our current theories of anesthetic uptake and distribution had simple beginnings. In his classic paper, Kety made several assumptions which permitted the first reasonable simulation of anesthetic uptake. One of these assumptions was that all tissues receive equal perfusion per unit volume. Kety was aware that this was incorrect, but to assume otherwise presented an almost overwhelming mathematical obstacle. Later, Price, then McKrell, Mapleston, Severinghaus, and Eger discarded this assumption and proposed new models which assumed differential perfusion of tissues (i.e., the visceral tissues receive a high flow, muscle less, fat still less). These analyses were made possible by the development of analog and digital computers. One by one the remaining simplifying assumptions made by Kety also have been abandoned in favor of more complex but more realistic assumptions. For example, the impact of ventilation/perfusion abnormalities on uptake has been analyzed. Similarly, the effect of varying inspired concentrations of anesthetic (the “concentration effect”) has been accounted for. We have calculated the effects of proportionate and differential changes in blood flow to tissues. Even anesthetic metabolism has its counterpart in simulation.

Several surviving assumptions are patently false, yet have remained unchallenged. Until the work by Ashman, Blesser and Epstein (A Nonlinear Model for the Uptake and Distribution of Halothane in Man) which appears in this issue of Anesthesiology, we had assumed that induction of anesthesia did not affect the initial physiologic conditions given the computer. Thus, ventilation, circulation, metabolism, etc., were presumed to remain constant once the initial conditions had been set: if we began with a cardiac output of 5 l/min, then we finished with a cardiac output of 5 l/min. As Ashman et al. note, this conflicts with reality. For example, halothane decreases cardiac output, and this decrease (at least initially) should decrease halothane uptake and thereby allow achievement of a higher alveolar concentration. Ashman and his co-workers addressed themselves to the problem of calculating the effect of a progressive decrease in output with increasing partial pressure of halothane. Their solution suggests that an hour of inspired halothane at 1 per cent produces an alveolar halothane concentration 6 per cent above that produced when cardiac output is constant. This is the first computation of the effect of an anesthetic on its own uptake through its influence on a physiologic variable. It therefore represents a significant advance over our previous assumptions.

Ashman’s paper points up the value of electrical and mathematical models that simulate...