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Editorial Views

CPPB and Vasopressin Secretion

CONTINUOUS POSITIVE-PRESSURE BREATHING (CPPB), defined as assisted respiration in which the end-expiratory pressure in the trachea is always greater than 0 mm Hg, is now being used more frequently as a method of increasing alveolar oxygen tension in individuals with respiratory insufficiency. In 1947, Drury, Henry and Goodman described decreased cardiac output, peripheral venous pooling, hemoconcentration, increased pulse rate, minor elevation in blood pressure, decreased urinary output, and decreased urinary urea excretion as a result of CPPB.[1] These changes were proportional to the duration of CPPB and to the level of end-expiratory pressure. They commented on the dangers of the body's sacrificing the kidney to maintain venous return and suggested that the depressed renal function has hormonal in nature, caused by increased antidiuretic hormone (ADH) secretion. They cited a paper by Brun, Knudsen and Raaschou, who had demonstrated that postsyncopal oliguria associated with the passive erect posture mimics the oliguria caused by injections of ADH.[2]

In a series of studies conducted during the early fifties, Henry and his colleagues used CPPB and its opposite, negative-pressure breathing, as experimental tools to engorge and deplete the thoracic blood volume in their search for the thoracic low-pressure volume receptors, which they finally located in the wall of the left atrium in and about the entrance of the pulmonary veins.[3] Because of the knowledge that changes in endotracheal and intrathoracic pressures might alter vasopressin secretion, most investigators subsequently studying the mechanism of vasopressin secretory control have tried to sidestep the problem by avoiding experiments in animals with open thoracic or abdominal cavities. Instead, they have confined their studies to conditioned conscious animals or to animals breathing spontaneously under extremely light pentobarbital anesthesia.[4]

In 1960, Baratz and Ingraham proved that CPPB produced an increase in plasma ADH levels and speculated about the relationship of CPPB to other potent stimuli of ADH secretion related to volume regulation.[5] Now, ten years later, employing a more specific and sensitive method for estimating plasma levels of ADH, Baratz and his collaborators have begun to report on a series of systematic investigations of the effects of respiratory mechanics on vasopressin secretion and the mechanisms involved.[6, 7] They have demonstrated that an end-expiratory pressure of 0 mm Hg (IPPB) has no effect on plasma ADH levels and urinary output when arterial P_{CO_2} is not altered. In their latest paper, "Plasma Antidiuretic Hormone and Fluid Balance during Continuous Positive-pressure Breathing in Dogs," appearing in this issue of the Journal, they have more carefully defined the increase in plasma ADH levels occurring with CPPB and have demonstrated that the low-pressure volume receptors of the left atrium are not involved.

Before I comment on specific points of their experiment, a brief summary of the vasopressin secretory control system is in order so that the effect of CPPB can be placed in its proper prospective. Readers seeking more details should consult two recent reviews[8, 9] and a more lengthy discussion of my personal bias to be found in reference 10.

The terms "antidiuretic hormone" and "vasopressin" are synonymous, and refer to an octapeptide called "arginine vasopressin" that has a molecular weight of 1,084. This substance

is produced in the neurosecretory cells of the paraventricular and supraoptic nuclei of the hypothalamus. Vasopressin and oxytocin combine with a polypeptide carrier, neurophysin, and migrate down the axons of these cells, which terminate in the posterior pituitary gland. Upon an appropriate stimulus, vasopressin is released into veins surrounding the posterior pituitary and carried down the jugular system, passing through the pulmonary system without being destroyed. It has a half-life in the peripheral circulation of about three minutes and is cleared from the blood in one pass through the hepatic circulation. About 10 per cent is excreted unchanged in the urine.

Vasopressin has three major actions on the kidneys which are related to dosage. At the lowest level a linear relationship can be developed with the reduction of free water clearance (CHOH) due to the distal tubular reabsorption of water without solute; hence, the name "antidiuretic hormone." As the level of ADH is increased the CHOH response becomes nonlinear and rapidly less effective. However, at these levels a linear relationship begins to develop with its reduction in urinary osmolal clearance (COSM). As ADH levels rise higher, the COSM response also becomes nonlinear and less effective. The reduction in COSM which is associated with a reduction in creatinine clearance is probably the result of a reduction in renal blood flow and occurs at ADH levels known to produce changes in regional blood flow. If ADH levels continue to increase all urinary flow will stop, due to constriction of the collecting ducts. Vasopressin also produces constriction of the walls of large vessels and other structures having smooth muscle fibers. It must be remembered that vasopressin is many times more potent as a vasoconstrictor than angiotensin.

At least three types of sensor systems are involved in the closed-loop control of vasopressin secretion. The first, the "osmoreceptor system," is sensitive to small changes in plasma concentration and can modulate blood ADH levels between 0 and 6 μU/ml. This also happens to be the range over which ADH is capable of restricting urinary flow through the mechanism of reducing CHOH. The osmoreceptors may be the hypothalamic neurosecretory cells themselves. The second closed-loop control system involves low-pressure volume receptors located in the left atrium of the heart, which can modulate blood ADH levels between 0 and 60 μU/ml. These sensors are connected to the hypothalamic neurosecretory cells through afferents travelling in the vagus nerves and affect urinary flow throughout the CHOH and COSM ranges. These sensors are active in positional changes of the body, isotonic fluid overloading, and nonhypotensive hemorrhage. The third closed-loop control system consists of baroreceptors located in the carotid sinuses and along the aortic arch. They are sensitive to changes in mean arterial pressure and can raise the blood ADH levels to 600 μU/ml or more. Both the vagus and carotid sinus nerves must be cut to inactivate these receptors.

The role of these three systems is to protect the central vascular volume. Their effectiveness and feedback control are governed by the range through which they can control vasopressin blood levels and the biological effect of the vasopressin level set. Thus, the concept of a hierarchy of closed-loop control can be developed. For example, the withholding of fluids would first activate the osmoreceptor system. If the reduction in CHOH were inadequate to protect central volume, the low-pressure volume system, and subsequently the baroreceptor system if hypotensive shock were imminent, would be activated. In the treatment of this severe dehydration each of these systems would be turned off in the reverse order, even to the extent of preventing accidental overhydration by allowing the excretion of large amounts of water with or without solute. Therefore, a normally-functioning vasopressin control system is a very important safety factor for those concerned with fluid therapy management.

The previously mentioned closed-loop hierarchy can be disrupted or confused in several ways by "noise." These mechanisms are called open-loop control. The loop can be opened by certain diseases of the renal tubules or by the giving of diuretics. The transfusion of banked blood which has been drawn in a manner such that the donor's baroreceptor system is stimulated confuses the system because of its inability to distinguish endogenous from exogenous ADH. The most frequent cause of open-loop stimulation is due to the structure of the hypothalamic neurosecretory cells them-

selves, which allows the reception of electrical stimuli through the limbic system both from the forebrain and from the reticular formation. Nonspecific mass discharges of nervous impulses secondary to emotional, somatic or visceral pain will cause a release of vasopressin not related to central vascular volume. In some types of visceral surgical operations, ADH levels as high as 150 μU/ml have been observed. This type of "noise" can be reduced by decreasing the stimuli or by blocking the input pathways. A slow methodical surgical procedure is often less stimulating than a fast rough procedure. Operative blood loss, on the other hand, does not confuse the system because transfusion or volume expansion will quickly reduce blood levels of vasopressin. However, if the open-loop stimulus of pain has raised blood ADH levels to 150 μU/ml, retransfusion will not eliminate the vasoconstrictive effect of the circulating vasopressin, thereby allowing the vascular system to be underfilled with subsequent embarrassment as the open-loop stimulus subsides or allowing overfilling with the partial loss of the ability to allow the escape of excess volume by the excretion of water and solute by the kidneys.

In this brief discussion of vasopressin secretory control and its role in the maintenance of central vascular volume, I have avoided mentioning all of the other neurohormonal control systems that are volume-sensitive. Some of these provide important routes of compensation when the ADH system is disabled by open-loop stimuli. Hyponatremia and hemodilution are avoided during these periods by giving intravenous fluids that contain solutes, such as balanced salt solutions.

The design of the experiment reported in this issue of the Journal was well conceived and executed. However, it must be pointed out that the plasma ADH levels obtained during periods of IPPB (10, 8, 10 and 15 μU/ml) are quite high. These levels are equivalent to blood ADH levels of 6, 4.8, 6, and 9 μU/ml, which are at the threshold where vasopressin alters COSM. The control plasma ADH levels in the two other reports are also high.[6, 7] These values are in the range where the urinary response is nonlinear, producing a large numerical change in plasma ADH concentration associated with a modest reduction in urinary output. Under these conditions the diuresis that was established must have had a fairly large COSM component and the elevated plasma ADH levels during CPPB primarily depressed the COSM component, as indicated by the decrease in urinary sodium excretion. I generally prefer to place the osmoreceptors and low-pressure volume receptors at rest during control periods, which means obtaining blood ADH levels of 0.5 μU/ml (plasma ADH 0.8 μU/ml) in the dog resting on his side. Similar values have been reported by Bonjour and Malvin.[11] Under these conditions the urinary output should have a large CHOH component. This point is not critical but probably prevented the response from being more dramatic.

It appears that CPPB in these experiments stimulated the baroreceptors and produced enough ADH to depress renal blood flow. Therefore, it functions within the hierachy that maintains central vascular volume by closed-loop control. However, it operates in the third and final loop, very close to the edge of decompensation. These authors might section the carotid sinus nerves as well as both cervical vagi during some future study, to be sure that baroreceptors are actually involved. I hope that they will continue to investigate this area and supply us with a definition of how to set a respirator so that vasopressin secretion is not affected.

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High-frequency Electrical Equipment in Hospitals

TRUSTING, indeed, is the surgeon who turns to scrub while the least trained member of the operating room team attaches the high-frequency electrosurgical instrument to the patient. Commonly misnamed "the cautery," surgical diathermy figures in more than a fourth of all incidents associated with electrical apparatus in hospitals—and the incidents tend to be grave: operating room fires and serious burns. The high-frequency electrosurgical instrument also limits choice of anesthetic agents, interferes with pacemaking, and frustrates effective ECG monitoring. Even when the device is inactive, its own circuits for "safety" and automatic operation inject "noise" into the ECG monitor and possibly hazardous voltages into the patient.

Granted that the electrosurgical instrument is the surgeon's tool and never is used by the anesthesiologist, no conscientious physician with a prudent regard for his patient's welfare can ignore a disruptive force intruding so impudently into the operating milieu.

Safety in the use of conventional 120-volt alternating current holds few subtleties. High-frequency electricity, however, is "another breed of cat." Preferring conventional conductors, yet able to ignore them if compelled to do so, it enjoys so many prerogatives under Ohm's Law as to seem exempt from control—if not uncanny. Moreover, the surgical diathermy is not a passive instrument; it is designed to destroy tissue, and is unselective. One is entitled to question the wisdom of an institution that entrusts this device to the uninitiated.

Even before the autumn of 1926, when Harvey Cushing and W. T. Bovie trundled their spark-gap machine down Shattuck Street to the side door of the Peter Bent Brigham to inaugurate a revolution in neurosurgery, electricity had been applied in general and urologic surgery. Despite a long history of use, however, good information about the ubiquitous and hazardous electrosurgical instrument has been difficult to obtain. "High-Frequency Electrical Equipment in Hospitals—1970," recently published by the National Fire Protection Association, is a signal event.* Designated NFPA No. 76CM, and assembled by a knowledgeable and experienced coalition of physicians and engineers, this manual provides essentials that should be appreciated by physicians, nurses, operating room supervisors, administrators, and engineering personnel concerned with high-frequency electrical equipment. The publication deals with properties of high-frequency circuits and their hazards, suggests protective measures, indicates administrative and maintenance considerations, offers sample regulations, and lists pertinent references. It is required reading for anyone who may be an accessory to the use of high-frequency electrical equipment in hospitals.

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* Available from the National Fire Protection Association, 60 Batterymarch Street, Boston, Massachusetts 02110, $1.00 per copy.