Meetings

Autoregulation of Blood Flow

The intrinsic ability of an organ to maintain the rate of its own blood flood relatively constant, when the arterial driving pressure for flow is changed, has been a controversial area of research, and recently was the subject of a research workshop involving experimental demonstrations, laboratory discussions, and formalized discussions. During a 5-day period, 26–30 November 1962, 14 representatives from the majority of American laboratories working in this field convened to discuss their findings. The first two days were spent with William Waugh (University of Kentucky); the latter three days were spent with Francis Haddy and Lerner Hinshaw (University of Oklahoma).

Six of the visiting participants brought their own apparatus and demonstrated their experimental techniques and results in the host laboratories. The experiments included ten different preparations which involved the circulation of the dog kidney, brain, intestine, skeletal muscle, and foreleg. In most instances the spectator investigators extended the original experiment to elucidate certain points of particular interest to them, and in many respects this was the most beneficial part of the tour.

Some physiologists have not observed the phenomenon of autoregulation of blood flow; while those who have observed it have not agreed on a probable cause. It seems possible that the wide variability in experimental results is due to the variety of experimental techniques employed.

W. H. Waugh (Kentucky) studied autoregulation in the isolated kidney with blood perfused by a donor animal. Small-vein pressures were measured by a catheter passed retrograde into the venous system. With large changes in arterial pressure, there were only small changes in small-vein pressure. Dissection of the kidney showed the catheter tip had not passed beyond the renal calyces. Data from other experiments in which the catheter tip was found in arcuate or interlobular veins showed similar changes in small-vein pressure. Waugh also reviewed his previous work which suggests that an active myogenic vascular response to the level of transmural pressure is the cause of renal circulatory autoregulation. G. Grupp (Cincinnati), in addition to Waugh, also stressed the influence of vasoactive agents on autoregulation of renal flow. He reviewed his work (i) on the relatively constant rate of renal oxygen consumption and heat production with changes in renal flood flow and (ii) on the shift from aerobic to anaerobic renal metabolism with short-term vascular occlusion.

H. E. Schmid (Bowman-Gray), using an electromagnetic flowmeter, studied flow regulation with acute changes in arterial pressure in the *in situ*, noncannulated kidney. He also reported the presence of autoregulation after kidney decapsulation. A blood-perfused, islolated kidney technique was described which showed that the autoregulatory resistance changes can be localized to the specific end-arterial vasculature of arteries in which pressure changes occur (R. B. Harvey, Minnesota). Additional reviews on renal circulatory autoregulation were presented by A. R. Koch (Washington) and F. J. Haddy (Oklahoma). Koch presented an analysis of the effect of varying the tonicity of the arterial blood and of the effect of osmotic diuresis on renal vascular resistance; and Haddy found that elevated arterial CO_2 tension did not abolish autoregulation in the kidney.

Experiments on the isolated kidney perfused from a heart-lung preparation showed changes in renal tissue pressure were largely responsible for the major resistance changes underlying renal autoregulation (L. B. Hinshaw, Oklahoma). Deep-venous pressure rose considerably with large elevations in arterial pressure, thus favoring the tissue-pressure concept. Identical deep-venous pressures were also measured by Waugh, who inserted a venous catheter of much smaller bore into the same preparation.

Recent studies of renal blood flow and glomerular filtration rate showed indirect evidence that the chief resistance changes underlying renal circulatory autoregulation are located in the preglomerular vasculature and that there is no significant redistribution of cortical and medullary blood flow with autoregulation (E. E. Selkurt).

In studies of cerebral blood flow by C. Rapela (Bowman-Gray) a blood pump was interposed in the arterial path and sometimes reduced or abolished cerebral circulatory autoregulation. However, hypercapnia is exceedingly effective in abolishing autoregu-

lation of cerebral blood flow by producing marked dilatation of resistance vessels. Rapela suggested that a very sensitive metabolic feedback mechanism (which perhaps tends to keep cerebral venous CO_2 tension constant) may be responsible for autoregulation of cerebral blood flow upon changes in arterial pressure.

R. M. Berne (Western Reserve) described the autoregulation of coronary blood flow and its absence in the fibrillating heart. He also suggested that such blood flow is controlled locally by myocardial oxygen tension, and this control appears mediated in part by the release of adenosine. R. D. Jones (St. Luke's Hospital, Cleveland) and Berne demonstrated intense circulatory autoregulation in the isolated thigh muscles which is sometimes impaired by incorporation of an arterial blood pump.

Additional demonstrations included preparations of (i) the isolated gastrocnemius-plantaris muscular vascular bed (W. N. Stainsby, Florida), (ii) the heart-lung-foreleg (Hinshaw), and (iii) the islolated intestinal loop (P. C. Johnson and K. M. Hanson, Indiana). The elevation of arterial pressure caused a large increase in blood flow followed by a slow return toward the control level in the isolated gastrocnemius-plantaris muscular bed. In this preparation the steady state vascular resistance decreased with arterial pressure elevation. However, other experiments have shown a direct relation between arterial pressure and vascular resistance. In Hinshaw's heart-lung-foreleg preparation, and in Haddy's dog foreleg preparation no autoregulation of foreleg blood flow was observed. The relative paucity of skeletal muscle vasculature in the dog foreleg, compared to foreleg skin and paw, was pointed out.

The last day of the conference was concerned with three main topics.

1) The group discussed criteria which should be applied to determine whether changes in tissue pressure are responsible for autoregulation. In an organ where the major resistance changes are due to generalized tissue-pressure changes, the greatest resistance changes should be found in those vessels most sensitive to collapse, such as the veins, while the pre-venous resistance will tend to remain constant. This type of autoregulation should be accompanied by sizable changes in interstitial pressure or lateral deep-vein pressure.

2) The group considered the expected behavior of a preparation ex-

hibiting myogenic autoregulation, a type which depends upon vascular transmural pressure. This response should exist only in vessels possessing active smooth muscle tone, or might be evoked in previously atonic vessels if they are sufficiently reactive to the stimulus, and should be abolished by any agent which paralyzes vascular smooth muscle. Such autoregulation may occur in the absence of a parallel change in tissue pressure, venous resistance, or organ weight. When venous pressure is elevated, total vascular resistance should increase except where capillary pressure is high (for example, in the kidney), or where tissue pressure increases substantially.

3) The group considered metabolic autoregulation. Generally, resistance is dependent on blood flow in a manner consistent with maintenance of an adequate nutrient supply. In comparing it to myogenic autoregulation it is similar in that it requires active smooth muscle tone and may be seen in the absence of parallel changes in tissue pressure, venous resistance, or organ weight, and dissimilar in that vascular resistance to blood flow should decrease with elevation of venous pressure.

Finally, the group discussed further experiments which should be performed to determine the nature of autoregulation demonstrated in the various organs.

The workshop was a most useful method to the participants in trying to resolve individual differences and in determining the areas most likely to be fruitful in this research field. It was generously supported by a grant (H-7124) to one of us (P.C.J.) from the National Heart Institute.

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Forthcoming Events

May

12. American **Pharmaceutical** Assoc., Miami Beach, Fla. (W. S. Apple, 2215 Constitution Ave., NW, Washington, D.C.)

12–13. **Biology** Colloquium, 24th annual, Oregon State Univ., Corvallis. (F. A.