higher volume is contained in the larger arteries of the bat wing. Less resistance to flow into peripheral areas is thus provided, but it becomes necessary to step down arterial flow and pressure in the relatively smaller vascular compartment here provided by the arterioles. It is perhaps not coincidental therefore that the rhythmical contractility seen in patagial arterioles (with a relatively small total cross-section) becomes extremely prominent, particularly at the level of precapillary sphincters.

The low pressure side of the vascular exchange bed (fig. 2) includes the venules (the so-called 'venous capillaries'). It is therefore far more extensive in bat wing than in dog mesentery. Increased potential area for resorption of interstitial fluids directly into the venous system might thereby be provided in a bat at rest if the downstream action of the contractile veins (with a relatively large total cross-section) tended to empty the venules. In flight however, at least with engorged capillary beds, a similar effect would seem at best to be capable of compensating somewhat for, paradoxically, a relatively greater fluid loss to the interstitium in a situation already favorably disposed toward edema. However, the accompanying lymphatics can likewise act over this expanded region and in themselves exhibit marked morphological specializations at their distal terminations as well as remarkably pronounced active rhythmic vasomotion. One wonders whether the implied high turnover of interstitial fluid in the wing during flight might be of advantage to a bat for such needs as thermoregulation.

A far greater proportion of venous volume of the bat wing is in small veins as opposed to larger ones (figure 2). Such a relationship seems entirely reasonable in terms of the energetic economy of a system in which blood must be returned toward the heart against centrifugal forces generated in flight, and over relatively long distances in any case; a higher intraluminal pressure can be generated by a given wall tension in a smaller vessel.

How important are the rhythmically active veins to the bat, relative to the other factors considered thus far? Like so much of the foregoing discussion, any rational answer to this question must remain a matter of speculation pending further experimental information. There is reason to believe that species differences can be considerable. And we must appreciate that present evidence has been obtained either from the passively outstretched wings of immobilized animals or from isolated vessels in vitro. It is known, for example, that intraluminal pressures in these veins can approach those in the arteries. On the other hand, I know of no attempts to assess actual pressures experienced by bat wing vessels during flight, against which to compare available in vivo and in vitro findings. Such data are sorely needed to better evaluate the overall contribution of active, rhythmic venous vasomotion to the total hemodynamic equilibrium of the wing.

A clearly effective neurogenic control over vascular tone has to date been demonstrated only in the larger arteries of the bat wing membranes. The vasomotion in the rhythmically contractile veins appears essentially myogenic, perhaps to a unique degree. The degree of nervous control over the shunt veins, digital arteriovenous anastomoses and vessels in the limbs proper is to my knowledge unknown. It might well be that a more rigorous comparison of such parameters in the bat might provide us with a far greater insight into factors which favor neurogenic as opposed to myogenic control of certain components of the cardiovascular system, and the ensuing advantages which thereby accrue to the total welfare of a successful organism. (For further discussion and references see Kallen, Biology of Bats, vol. III, chapter 3. Academic Press, New York 1977).

Functional characteristics and physical limitations of the active venous pulse in the bat wing: The effects of pressure and temperature

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Almost a century has past since Luchsinger[1] attempted to examine flow in the bat wing by perfusing it with bovine blood. Since then, the subcutaneous wing vessels of the bat have become a classic model for the investigation of rhythmically active myogenic activity in small blood vessels. In this model, the metarterioles and precapillary sphincters (whose cells are not contiguous) exhibit an asynchronous rhythmic form of vasomotion which stems from the activity of independent pacemaker units, the location of whose focus may, possibly, vary from time to time. On the other hand, the larger veins and venules, which possess continuous muscle coats and are capable of cell to cell propagation, display a more synchronized myogenic pattern of activity which is limited to well-defined independent functional units lying between 2

valves. It is conceivable that the spread of excitation between segments of the larger vessels is prevented by a barrier in the valvular area (possibly in the form of a more restricted number of muscle cells located there), particularly since the work load due to incoming tributaries, and consequently the pattern of vasomotion, is often found to differ in each segment.

The ability of blood vessels to adjust their flow constantly, irrespectively of the activity of the heart, is generally attributed to the inherent property of certain vascular smooth muscle types to respond directly to changes of tension in the vessel wall. The finding in various smooth muscles (as well as, from our own observations, in metacarpal bat veins) that even a slight increase in longitudinal force is associated with an increase in spontaneously generated spike potentials and tension development, indicates that myogenic responses are closely associated with cell membrane stability. The exact manner in which 'stretch' elicits cell depolarization in any smooth muscle, however, has not been truly elucidated, though chronic denervation and local anaesthesia have been used in many tissues to rule out the possible participation of a nervous action in governing these reactions. We have shown[2] that the denervation of 'anastomized' metacarpal veins (i.e. which are free from contiguity with the arterial pole) leads to a pronounced loss in tone and a reduction in both the frequency and the amplitude of rhythmic contractions. More recently[3] we have also measured the changes of pressure that are produced within metacarpal veins when their adjoining nerve bundle is electrically stimulated. Though the results of such experiments may demonstrate the ability of the nervous system to adjust both the basal tone and blood flow of these vessels, they do not imply a neurogenic origin to the 'stretch response'. Whatever the nature of the respective target and effector systems for the myogenic response, the view that transmural pressure is intimately related to blood flow autoregulation has remained largely unchallenged. Speden[4] has put forward an interesting idea, whereby the cell membrane of the vessel wall itself might comprise a 'length sensor' unit in parallel with the contractile elements. Such a system would, in fact, readily explain how a negative feedback is established after muscle contraction has developed, and yet still remain in agreement with the general findings that the myogenic responsiveness of vessels to changes in transmural pressure is most often parallel to their level of basal tone. Folklow and Neil[5], likewise, have compared this process to a 'spontaneously active mechanoreceptor with a built-in contraction system', whose negative feedback, in this case, would be largely furnished by the vasodilatory influence of released metabolites. This problem may be more complex, however, when one considers that even small variations in the transmural pressure, produced, for example, by respiration, changes in posture, and muscle contraction, may cause substantial changes not only in the geometry of the vessels, but also in their state of stress, and in the elastic and visco-elastic properties of the walls (see e.g. Attinger[6]), all of which can strongly affect the distensibility of the vessels. Consequently, it may well be thought rather unwarranted to regard either 'wall tension' or 'vessel caliber' as the primary factors regulating or being regulated by the myogenic response. These considerations, which contribute to the difficulty of defining the dynamic properties of all veins, are even more pertinent when applied to the study of rhythmically active vessels, where regular patterns of contraction and dilatation are superimposed on the graded changes in 'contracture tension' which are normally associated with variations in basal tone.

We shall not attempt to describe in this article the pioneering studies of such authors as Mislin, Wiedeman, Nicoll and Webb, and others, through which the autonomic nature of rhythmical vasomotion in the bat wing was first established. They have recently been extensively reviewed, clearly analyzed and woven together by Frank Kallen in vol. III of 'Biology of Bats' (Ed. Wimsatt, Academic Press 1978). It will suffice for our purpose to refer to those of our observations which exemplify the difficulties of analyzing pressure-volume and flow velocity data in such models and, some of our own attempts to overcome them.

Since the venous walls at the metacarpal level are very thin in relation to their radius, and as they contain a significantly lesser number of elastic elements than is the case in corresponding arteries, they are not, mechanically speaking, 'self-supporting'. Consequently, the cross sections of a venous segment may oscillate between complete collapse and full distension depending on the interplay between intra- and extravascular forces in relation to the stiffness of the walls at any given time. This, of course, would have been an irrelevant consideration had the transmural pressure always been sufficiently large to prevent collapse. Huggel's measurements of Megachiropteran interdigital veins[6] have shown, however, that very low pressures (around 9–10 cm H_2O) can prevail naturally in situ at certain periods, and one might be tempted (as we were at first) to analyze flow data as a function of perfusing pressure at similar values. This factor, however, can introduce considerably theoretical and practical problems, the understanding of which are important to the interpretation of venous function and control in the bat wing.

A pressure-volume curve which is obtained from a dilated venous segment is usually curvilinear with convexity towards the pressure axis. The rise in pressure causes an increase in radius and a decrease in wall thickness, and the wall tension thus increases out

of proportion to the increase in pressure. When the fluid is added to a 'collapsed' vein, however, the vessel must first regain its circular cross section which it will do without increasing its circumference or stretching the walls. In this case, the resulting pressure-volume curve will be sigmoid in shape. The first part, associated with the initial volume increase, will exhibit a rapid rise in pressure. In the middle part the change in pressure will be small compared to the volume change, and in the final stage pressure will again rise steeply with a minimal volume change. The rise in pressure which is recorded in the early phase need not, however, be accompanied by a significant increase in the tension of the walls, since the load against which the muscle contracts, according to the Laplace relationship, is determined not only by the transmural pressure but also by the radius (or configuration) of the vessel. Consequently, when the pressures that are applied to such collapsible vessels remain below a minimal threshold value, the concomitant increases in expulsion of blood at each pressure rise are small and difficult to relate numercially to prevailing conditions. As the vein is progressively filled, the muscle elements become increasingly efficient in developing force until, finally, the active components of muscle tension become unable to operate against the high transmural pressure which exists in the highly distended state. These considerations have led us to focus our attention principally on what we have termed a 'physiological range' within which the elastic moduli change with somewhat greater predictability with each stepwise increment in perfusing pressure, thus allowing for a clearer assessment of the active role of the muscle elements in actually assisting autoregulation.

The relatively high optimal range of approximately 25–60 mm Hg at which we have found the metacarpal vein to develop maximal active force may well be related, according to Kallen[7], to the animal's adaptation to flight. Within these limits the myogenic autoregulation of blood flow is most effective and corresponds to the range in which flow remains largely unchanged in relation to perfusion pressure, an almost linear relation being preserved between these two. Beyond this range, flow rate increases more dramatically, as does the circumference of the vessel despite the fact that the amplitude of contractions becomes negligible at this time. One might imagine, following this observation, that vessel caliber is the primary factor determining flow rate. However, at times when the process of 'rhythmical vasomotion' is impeded (e.g. following the perfusion of calcium-free EGTA physiological solution at moderate pressures) flow is considerably reduced, despite the pronounced increase in vessel diameter which is also prevalent at this time. This demonstrates that the rate of flow in the metacarpal veins of the bat is not only influenced by, but is very much dependent upon, an active rhythmical process of vasomotion rather than on the sole ability of the vessels to act as passive conducts. If these segmental contractions are to develop a sufficient propulsive force, they must be assisted by a proper functioning of the intersegmental valves. The functional contribution of these in bat alar veins may be simply to increase the efficiency with which intramural forces act as an auxillary pump to propel the blood towards the heart. Muscular activity would, in this case, be transformed into 'flow energy' by the production of an immediate resistance to reverse flow after each muscular contraction.

The body temperature of homothermous animals is governed to a great extent by the factors which determine the rate at which heat is lost to the environment. The presence, in Chiroptera, of a disproportionately large wing surface area in relation to body mass, though certainly valuable in assuring the rapid dispersion of heat during flight, must also account for a poor insulation when the ambient temperature decreases below a certain value. The majority of bat species are noteworthy, in fact, for allowing their body temperature to fall regularly, during their daily periods of inactivity, to levels that approach those of their surroundings. Kulzer et al.[8] have suggested that this characteristic may be related to a very early development of heterothermia, and thus have been an important prerequisite for the evolution of natural hibernation in the cool temperate zone, well before the different species emigrated to various continents. Kluger and Heath[9] have attempted to associate this distinctive feature with an inherent variation in the normal pattern of the central nervous organization that is habitually present in other mammals.

As concerns the purely local mechanisms that control circulation in the bat wing, temperature, along with pressure, is a factor of vital importance in that it affects directly the contractile activities of vascular smooth muscle that lead to changes in vessel tone and rhythm of spontaneous vasomotion which assure the peripheral regulation of blood flow. The predominantly chemical nature of muscle contraction at this time is affirmed through the close adhesion of the rate of rhythmic vasomotion to the Arrhenius equation. The reported Q_{10} values (1.8–2.4), whether measured in vivo or in isolated vessels, mostly fall into the predictable range for biological reactions. One exception to this is reflected in Wiederhielm's[10] results (3.1–4.7), which were obtained as a result of warming a section of venule in the intact wing with a radiant heater. Our own obervations in vitro (10 experiments), with the larger metacarpal veins of *Pteropus giganteus,* give a Q_{10} of approximately 1.8–2.6 for changes of temperature extending over a range of 15–35 °C. These values did not differ significantly in vessels that were induced to contract again (5 out of

10 attempts), after having been kept for 48 h at 7 °C in a physiological solution which was oxygenated twice each day. Below 4 °C and above 45 °C isolated vessels lost their ability to contract rhythmically. In the upper temperature range, at any rate, this is most probably due to an irreversible protein denaturation.

The difficulty of presenting, at this moment, a complete working model for the autoregulation of blood flow in the bat wing is relevant to nearly all other vascular territories. Any such endeavour must take into consideration not only the functional characteristics of the smooth muscle elements and other close lying structures, but also the superimposition of nervous (reflex and central), hormonal and metabolic influences, which are present at all times. Nevertheless, it is hoped that some of the problems raised in this paper may be considered as an initial contribution to this study as well as a starting point for further investigation. The bat wing lends itself as a particularly well suited model to the study of these parameters.

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Histology of the vascular wall and its innervation

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Mammalian veins have been categorized according to their fibre content. Accordingly, there are 3 large groups of veins: fibrous, fibroelastic and muscular. This latter group has been further subdivided into fibromuscular and musculoconnective.

The metacarpal vein of the bat is classified, along with veins such as the plantar, tibial, spermatic, internal iliac, hepato-portal, etc., with the musculoconnective type of muscular vein, because of the presence of loose collagenous bundles and a predominance of helicoidal muscle cells in the media[1].

Histology of the venous wall

a) The *neurovascular bundle,* composed of a mixed nerve located between a muscular artery and vein[1,2], is ensheathed by connective tissue composed of both cellular and fibrous elements[1,3]. This sheath, which jackets the neurovascular structures, anchors the components to the metacarpal bone as well as the dermal elements of the upper and lower wing membranes. The *metacarpal artery* feeds small arteries and arterioles that are accompanied by adrenergic nerve fibres. The *metacarpal veins* receive blood from small muscular veins. Valves, which regulate the influx of venous blood, are found at the juncture of vein and small vein[3,4]. Valves, however, are not restricted to these junctures. They are also found strategically placed at nonjunctional segments. No report of a vasa vasorum in the arterial or venous wall has been noted.

b) *Non-nervous composition of the venous wall.* From the earlier articles to the present it has been agreed that the vein is composed of 3 distinct layers[1,5]. The intima is lined on the luminal side by tall endothelial cells (figure 1). These cells lie on an amorphous matrix that seems to lack muscular cells or even connective fibres. However, elastic fibres from the media do pierce this inner layer and accumulate at the base of the valves, some of which later may extend into the valve leaflets.

The venous valves are seen as a single flap[3] or composed of 2 connective leaflets[1,3]. These valves appear as connective outgrowths of the intima[1]. Their nonfibrous bodies are supplemented with few cells and rare elastic fibres at the base of the valve. Typically, they are lined with endothelial cells, thus presenting a continuous surface to the lumen. The overall thickness of the intima is between 3.5 and 5.7 µm[1].

Underlying the intima, and delimiting it from the media, are evenly spaced elastic fibres running the length of the vessel (figures 2 and 3). Here, quite atypically, the elastic fibres are not fused into an internal elastic lamina, but are closely aligned to form an elastic boundary[1].

The media is the thickest coat, being 20–30 µm thick. Here, the muscle cells form 3–4 layers of helicoidal or annular elements (figure 3) running in a circular orientation[1,5,6]. Running between the muscle layers are bundles of collagen fibres (figure 4). These crisscross in a general longitudinal direction and form a loose meshwork of variable thickness. Elastic fibres, lying in the longitudinal plane are seen in the media (figures 5 and 6). They are not numerous here and