channels of the sarcoplasmatic reticulum very often connect the cell surface with the accumulations of mitochondria of the central area. Such connections are particularly developed in the peripheral muscle cells of the media, that is in the region of neuromuscular synapses (figure 2, c–e). The findings of other authors on vascular smooth muscles[10,12] suggested employing strontium as a tracer to show that the sarcoplasmic reticulum of smooth muscles plays a role similar to that of striated muscles. It functions as a source of activator calcium and a site into which calcium is actively accumulated during relaxation[4,10]. On account of these authors' findings there is every reason to believe that the extensive sarcoplasmic reticulum, especially the straight channels mentioned above, functions as the passage for a fast influx of Ca.

The pharmacochemical trigger mechanism, which activates the contractile apparatus by causing a rise in intracellular free calcium, is realized by the neurotransmitter substances of numerous nerve endings in the contact area of t. adventitia and t. media. These are polyaxonal, nonmyelinated nerves entering jointly with the vasa vasorum into the t. adventitia but not into the inner t. media. Near the synaptic area, the Schwann-cell sheath is partially opened and connected to the glycocalix of processes of the muscle cell by a web of collagenous fibres and reticular filaments, so that a permanent synaptic contact is given (figure 2, c–e), which is independent of the contractile status of the vessel. However, the intersynaptic gap seems to be variable (0.2–1.0 µm). It changes in dependence of the contractions of the muscle cell. This type of a neuromuscular synaptic relation seems to be embodied in nearly all vertebrate vessels investigated so far and has been called 'the synapses at distance'[13]. The terminal axoplasm contains neurotubuli, some few mitochondria, as well as synaptic vesicles of different sizes with and without dense cores. Since special fluorescence microscopical or histochemical results concerning the type of nerve endings in the patagium veins, have been published the granulated vesicles only give an indication of an adrenergic resp. the nerve endings with clear synaptic vesicles to an cholinergic innervation of the muscle cells in the peripheral vessel wall. The central, in general not directly innervated muscle cells of the inner media probably seem to be stimulated by an electrical trigger mechanism beginning in the peripheral, nervously controlled muscle cells[14–16]. The numerous closed interdigitations (figure 1, b) with gap junctions between the muscle cells could be an important prerequisite for such a mechanism.

These very close connections of the muscle cells, the well developed system of sarcoplasmatic reticulum, such as the channel system of Ca^{++}-influx, combined with the high content of electron dense sarcosomes are the most remarkable characteristics of this vessel type, i.e. the ultrastructural substrate of its intrinsic myogenous automaty which has been demonstrated by the in vitro pulsations of the isolated vessel[1–3,14].

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The chemical and pharmacological milieu

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Although the bat can hardly be considered to be universally popular as an experimental laboratory animal compared to rats, cats, dogs or rabbits, there are many important and specific ways in which this highly developed mammal can be used to advance our knowledge.

A list of the advantages of the bat as an experimental animal should include the ease with which the wing vasculature can be observed microscopically and the fact that no anesthesia or surgery is needed for in vivo microscopic observation. The small laboratory space needed for storing the animals and the minimal effort required to maintain them is an advantage. Most importantly, there are many aspects of the cardiovascular system which can be studied encompassing such diverse areas as the architectural structure of the

vascular tree, mechanisms which control blood flow in distal areas, the determination of peripheral resistance for the maintenance of systemic blood pressure, and the responses of the various vessels to drugs and chemical agents. Among the disadvantages are the inability to use the animal easily for chronic studies and the small size of most obtainable species of bats which makes certain parameters difficult to measure. Bats are not usually listed by the suppliers of laboratory animals, so investigators must locate natural sources.

The blood vessels of the bat wing have been used for a variety of interests centered around anatomical, physiological, and pharmacological features. The clarity of the vascular field which can be achieved for visualization through the microscope at high magnifications is a most advantageous feature and has permitted investigators to describe important relationships between arteries, veins, lymphatics and nerves in a single vascular bed. The location of valves in venous and lymphatic vessels has been determined. The distribution of vascular smooth muscle cells has been demonstrated through staining with vital dyes or by observation of their contractile activity with or without external stimuli. The sites of spontaneous contractile activity in arterial and venous vessels have been documented.

Important mechanisms related to the control of blood flow into the capillary network are believed to be functioning normally in this unanesthetized mammal, and experimental efforts have resulted in some new concepts as well as the confirmation of postulated controls. For example, some controversy has existed regarding the means by which contractile activity of arteriolar vessels just proximal to the capillary vessels was initiated. Several possibilities were suggested such as nervous control, metabolic control, or myogenic control. Although the controversy is not completely resolved, it appears that nervous control is absent and that arteriolar vasoconstriction at this level is dependent on local factors such as metabolites and intraluminal pressure. It should be noted that these 2 factors are the bases for the theories of autoregulation.

As technology advances, so do the experimental approaches. Just recently it has become possible to measure the velocity of blood flow in the microvessels of the bat wing and other small animals, and through this, to establish the presence of pulsatile flow in this area of the arterial tree, heretofore said not to occur beyond certain relatively large arterial vessels. A reliable non-invasive method for determining blood pressure in the microvasculature remains to be developed, although pressure measurements have been made in arterial, venous, and lymphatic vessels of the bat wing.

Responses of arterial and venous vessels to drugs and to toxic materials have been studied in numerous in vivo preparations which permit microscopic observation. Vasoactive agents such as epinephrine, acetylcholine, and serotonin which occur normally in the body have been studied to demonstrate the vessels which are responsive to them. The site of action and effect of adrenergic blocking agents, anti-hypertensive, and anti-inflammatory drugs such as phenoxybenzamine, dipyridamole, and hydrocortisone on the vascular bed have been investigated. The effects of radiopaque materials commonly used in angiography have been studied in searching for an insight into the occasional toxic responses that occur in patients. It was determined through in vivo microscopic studies that the crenation of red cells, the accumulation of platelets, and the initial vasodilation followed by vasoconstriction that is a consequence of the introduction of a bolus of contrast agent into the microvessels was related to the osmolality of the preparation. As a result, a new type of contrast material with a compatible osmolality has been developed and is now being used clinically.

A new area of investigation is directed toward the adhesion and aggregation of platelets to arterial and venous vessels following external stimuli such as heat from a single pulse laser beam or an electrical current delivered through microelectrodes. It is possible to follow the initiation and development of the platelet aggregate and also to study the influence of selected drugs designated as inhibitors or enhancers of platelet aggregation. One of the interesting facets of these studies is that differences have been revealed between in vivo reactions in the unanesthetized animal and in vitro or ex vivo reactions. Several hypotheses have been put forth based on changes in platelet activity observed in vitro such as platelet shape change indicating the initial response that renders the platelet adhesive. A shape change is not always seen in the living animal prior to or during adherence of platelets to one another or the vessel wall. Furthermore, collagen takes an active part in aggregation of platelets in the test tube as recorded by an aggregometer. From this reaction, it was concluded that exposure of collagen in the vessel wall which underlies the endothelial lining was a prerequisite for platelet adherence. In vivo studies in the bat wing showed platelet adhesion and aggregation in the absence of collagen exposure.

Platelet activity was also found to be the leading cause of ischemia that developed following i.a. injections of an oral barbiturate. The information should have clinical importance because of the recent problem of inadvertant i.a. injections of secobarbital by drug addicts which frequently is followed by gangrene in the fingers and hand of the injected limb. In addition, a similar problem is occasionally seen in the operating room when sodium pentothal is mistakenly given i.a. The clinical signs led to the speculation that arterial vasospasm was responsible for the damaging results,

but direct microscopic observation of bat wing arterial vessels following barbiturate injection showed platelet aggregates at arteriolar branch sites blocked flow into the capillary nets with the absence of arterial constriction.

Other studies relative to medical problems include observation of bat wing vessels in response to ethyl alcohol, both injected and ingested, to ascertain the vascular responses to various concentrations in the blood stream and an investigation to learn the mechanisms by which cold water acted to alleviate the pain and edema caused by 1st and 2nd degree burns of skin.

It is obvious from this brief review of the specific investigations in which the bat wing vessels have been used as the experimental site, that the bat, unanesthetized and with an unaltered cardiovascular system, lends itself to a wide variety of studies that have a direct application to the understanding and treatment of medical problems. The list presented here is not complete, but indicates the present and potential usefulness of the bat as an experimental animal.

Interaction of Ca and K ions in governing spontaneous electrical and mechanical activity of bat wing veins

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The usefulness of blood vessels, that display rhythmically active vasomotion, in studying the mechanisms concerned with vascular smooth muscle activity, has now been adequately demonstrated. Bat wing vessels may present an additional advantage to several other models, in that they are easily accessible for comparative investigations in situ[2]. The aim of the present study was to determine the role of potassium and calcium ions in governing the electrical and mechanical events associated with spontaneous vasomotion in bat metacarpal veins. A sucrose-gap technique such as previously applied to the analysis of normal electromechanical coupling in the smooth muscle of such vessels was used for this purpose[3].

In the bat vein, this activity is essentially composed of single plateau-type action potentials (which occur at regular intervals), each of whom is accompanied by a contraction-relaxation cycle, measured in vitro as an isometric change in longitudinal force. During normal activity action potentials may be seen to arise either abruptly from a steady membrane potential (figure 1, A), or as the consequence of a slow wave of depolarization, resembling pacemaker activity, which rises to the threshold level of the following action potential (figure 1, B).

A segment of vein between 2 valves and approximately 2.5 cm in length was dissected from the neurovascular bundle, ligated at both ends, and allowed to rest for 1 h in normal C.S.3. physiological solution[4]. The vessel was then mounted in a sucrose-gap apparatus. One end was fixed and depolarized with high-K^+ solution, and the other end, which was connected to a force transducer (Grass FTO3), was bathed in normal C.S.3. solution at 35 °C. The section of muscle lying between the recording electrodes was superfused with isotonic sucrose solution. A passive tension of approximately 200 dyn/cm^2 was applied to the muscle before each experiment. Solutions with increased K^+ content were prepared by replacing NaCl with equimolar amounts of KCl, whereas K^+-low and K^+-free solutions were obtained by substituting sucrose for KCl on an equiosmolar basis. Variations in Ca^{2+} were compensated by corresponding equimolar changes in sucrose content. All solutions were aerated with a gas mixture of 97% O_2 and 3% CO_2. The pH of the solutions was adjusted as necessary to a value of 7.4 by the addition of a small quantity of H_2SO_4.

The total removal of K^+ from the bathing medium was followed by a brief increase in the frequency of spike firing, and a reduction in the duration of the plateau phase and of the quiescent period (figure 2). During this time additional spike components could be seen in some veins to accompany each action potential. Portal vein preparations have similarly

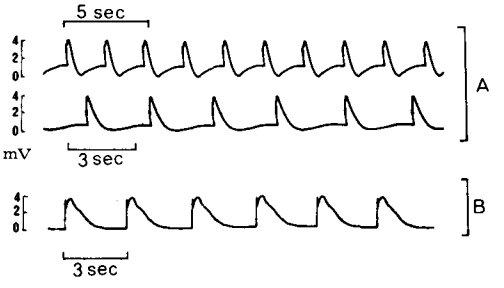

Fig. 1. 2 major types of electrical activity recorded in the bat metacarpal vein. *A* Repetitive-firing action potentials are each followed by a slow depolarization rising to the threshold level of the following action potentials. *B* Action potentials arise abruptly from a steady membrane potential without any preceding slow depolarization. The latter has been called a 'driven' as opposed to a 'pacemaker' activity.