along with their isotopic signatures, a more adequate budget may be constructed. The present measurements establish both a source magnitude and isotopic composition. In consideration of the participation of N_2O as both a catalytic ozone destructive agent and a greenhouse gas, definition of all sources, particularly those which may now be unrestricted, is clearly important. Our analysis suggests that in the long term it may be desirable to develop catalytic oxidation methods that avoid the stoichiometric use of nitric acid as an oxidant.

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Distinctive Cranial and Cervical Innervation of Wing Muscles: New Evidence for Bat Monophyly

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The traditional view that Old World fruit bats (Megachiroptera) and insect bats (Microchiroptera) are closely related has been challenged by claims that Megachiroptera are the sister group to flying lemurs (Dermoptera) or Primates. We found that the specialized muscles of the rostral part of the wing in Microchiroptera and Megachiroptera receive double innervation by both the facial nerve and cervical spinal nerves, suggesting that bats are monophyletic. Innervation by the facial nerve also occurs in Dermoptera and suggests that bats and Dermoptera share a common ancestor that had wings.

BATS (CHIROPTERA) ARE THE ONLY mammals that fly actively, and this locomotor behavior has exerted a pervasive influence on their evolution. A striking aspect of wing morphology is the presence of a specialized muscle complex, sometimes called occipito-pollicalis in bats, that extends along the rostral part of the wing (propatagium) and is absent in quadrupedal mammals (*1*) (Fig. 1). This propatagial muscle complex has been used as evidence for the monophyly of bats (*2*) and to demonstrate close phylogenetic ties between *Cynocephalus* (Dermoptera) and bats (*3, 4*). But the complex is also present in other winged vertebrates that are not closely related, such as the flying squirrel *Glaucomys* (*5*) and many birds (*6*). This suggests that the complex evolved independently in unrelated flying and gliding vertebrates and, thus, may devalue its presence as a supporting character for the monophyly of Micro- and Megachiroptera. Elimination of characters related to aerial locomotion has been used to support claims based on independent evidence that Megachiroptera are more closely related to Primates than to Microchiroptera (*7, 8*).

We used innervation as a criterion for establishing muscle homology because of the close link between innervation and muscle development. Resulting hypotheses of homology form a test for existing cladograms of the phylogenetic relations among archontan mammals (Recent Megachiroptera, Microchiroptera, Dermoptera, Scandentia, and Primates). We studied the innervation of the elements of the propatagial muscle complex using gross dissection and histological serial sections because previous reports are few and inconsistent (*3, 9*). We determined the innervation in the dermopteran *Cynocephalus volans*, the megachiropteran *Pteropus sp.*, and the microchiropterans *Myotis lucifugus* (Vespertilionidae) and *Tadarida brasiliensis* (Molossidae).

The results of our investigation are summarized in Fig. 2. The propatagial muscle complex of *Cynocephalus* consists of two layers extending perpendicular to each other and innervated by different nerves: the dorsal layer by cranial nerve VII and the ventral belly by one or more cervical spinal nerves. In *Pteropus*, five muscle bellies make up the propatagial complex. Four of the bellies are innervated by both cranial nerve VII and cervical spinal nerves. The remaining pectoral belly is innervated by cranial nerve VII and the pectoral nerve. Only two muscle bellies are present in *Myotis*; both are innervated by cranial nerve VII and cervical spinal nerves. The occipital, brachial, and distal bellies of the propatagial muscle complex of *Tadarida* are innervated by cranial nerve VII only, and its pectoral belly is innervated by the pectoral nerve only.

The innervation of the propatagial muscle complex is unusual for two reasons. It is the only known case in which voluntary limb muscles are innervated by cranial nerve VII. In addition, the dual innervation of the propatagial complex in *Myotis* and *Pteropus* by both cranial nerve VII and cervical spinal nerves is unique among mammals. The cell bodies of cranial nerve VII generally reside in the pons and medulla oblongata (*10*) and are not continuous with those of the spinal nerves. Innervation by a combination of nerves from the brain and spinal column has not been reported for any other mammalian muscle. A superficially similar case of dual

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innervation concerns the mammalian trapezius and sternocleidomastoid muscles that are innervated by cranial nerve XI and cervical spinal nerves (*11*). However, the axons from cranial nerve XI that innervate trapezius and sternocleidomastoid arise from nuclei in a motor column continuous with that of the spinal cord and merely travel with the cranial nerve extracranially.

The observed pattern of innervation has far-reaching implications for ontogeny. Muscles of the adult arise from migrating segmental mesoderm of the embryo, and the nuclei of nerves that innervate these muscles generally retain their original position and thus record the body segment from which the migrating myoblasts originated. The innervation of a voluntary muscle by branches from cranial nerve VII indicates that portions of this muscle developed from myoblasts of the second brachial arch (= somitomere six of the embryo) and innervation by

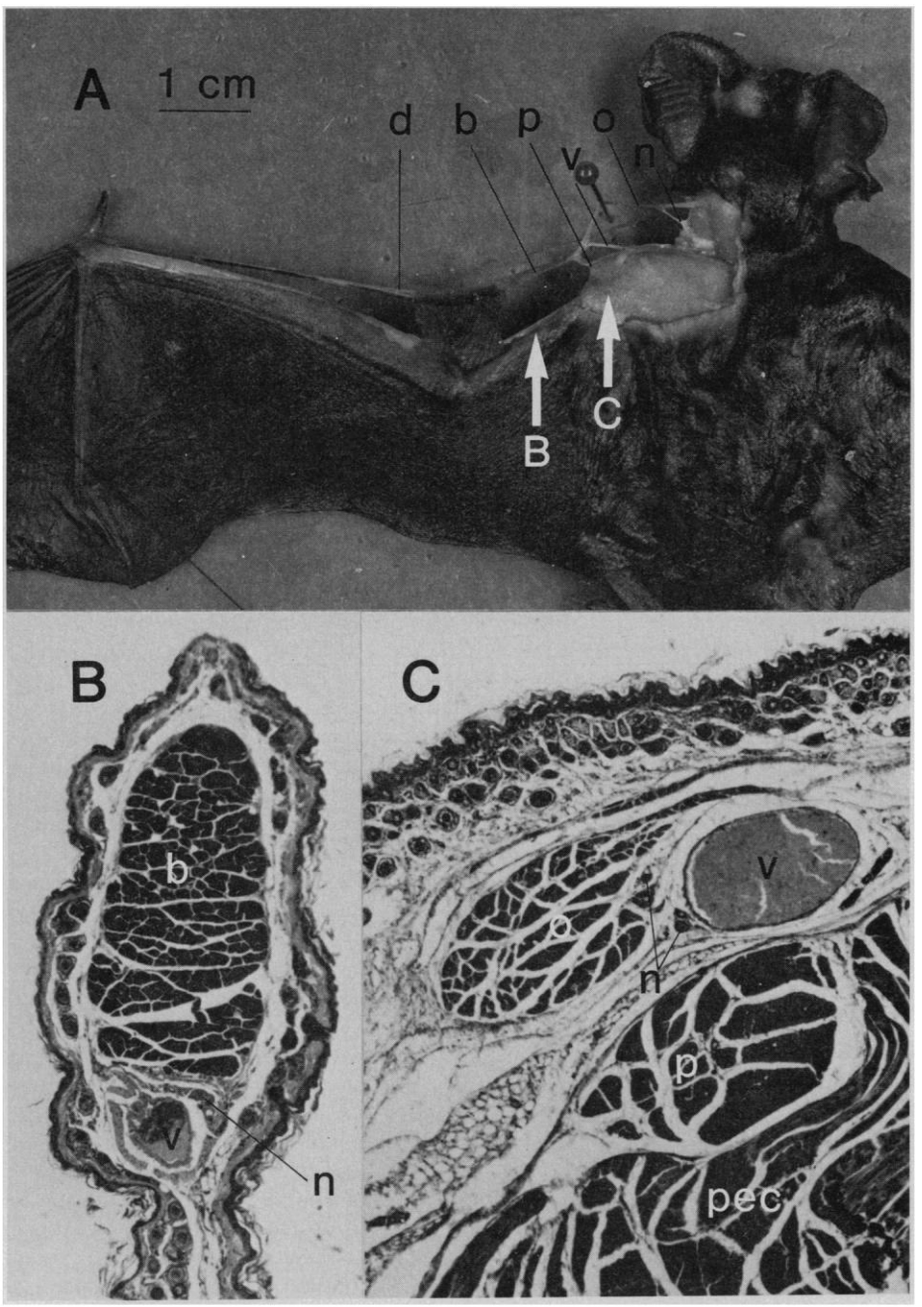

Fig. 1. The propatagial muscle complex in the microchiropteran *Tadarida brasiliensis*. Gross dissection showing (**A**) overall structure of the muscle (pulled away from the shoulder for clarity) and histological cross-sections at level of (**B**) brachial muscle belly and (**C**) shoulder. Arrows in (A) indicate approximate levels of histological sections of (B) (slide C 52-4) and (C) (slide B 74-7). Four muscle bellies contribute to the propatagial complex in *Tadarida*: distal (d), brachial (b), pectoral (p), and occipital (o). Branches of cranial nerve VII (n) innervate all bellies of the complex. The cephalic vein (v) extends along the caudal border of the complex. Some segments of the vein are bloodfilled [black in (A)]. Pectoral muscle is also visible in cross section (pec). Scale bar for (A) only. Rostral is toward top of page.

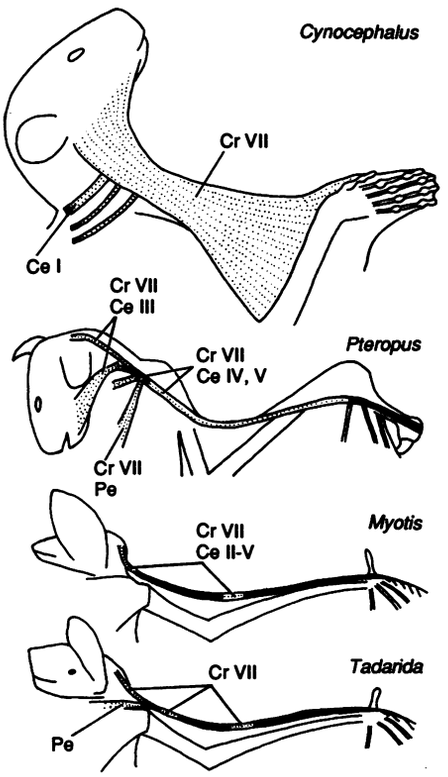

Fig. 2. Diagrams of structure of propatagial muscle complex and its innervation in *Cynocephalus volans* (Dermoptera), *Pteropus sp.* (Megachiroptera), *Myotis lucifugus* (Microchiroptera), and *Tadarida brasiliensis* (Microchiroptera). Muscle bellies in propatagial complex are stippled; collagenous and elastic tendons are black. Cr, cranial nerve; Ce, cervical spinal nerve; Pe, pectoral nerves. (Not to scale.)

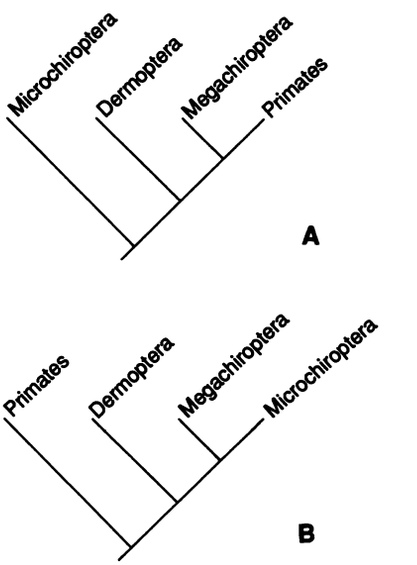

Fig. 3. Two current phylogenetic hypotheses for relations among Archonta. Cladogram A is based on figures by Pettigrew *et al.* (*8*, figures 8 and 17) and cladogram B on one by Wible and Novacek (*2*). Evidence from the propatagial muscle complex is more consistent with cladogram B, identifying synapomorphies for the node joining all of Chiroptera as well as the node joining Dermoptera and Chiroptera.

cervical nerves (as well as cranial nerves X to XII) indicates that other portions have an ontogenetic origin from cervical somites (*12*). Therefore a dual pattern of innervation suggests a complicated ontogenetic development of the propatagial muscle complex.

This pattern of innervation supports the monophyly of Mega- and Microchiroptera. On the basis of available evidence and current cladograms for archontan phylogeny (Fig. 3), two possible scenarios of the evolution of the propatagial muscles are possible. The innervation by cranial nerve VII and several cervical spinal nerves may have arisen twice: once in the branch of microchiropterans leading to *Myotis* and once in megachiropterans (consistent with both cladogram A and B) (*13*). Alternatively, the pattern may have arisen only once in the common ancestor to all Chiroptera, which is most consistent with cladogram B. These two scenarios are equally parsimonious in cladogram B, but we suggest that the rare developmental pattern that led to the dual innervation of the propatagial muscle complex and its possible mixed developmental origin make the independent origin of the pattern unlikely. If the distinctive innervation of the propatagial muscle complex evolved only once, cladogram B is corroborated by our data.

Our observations also have implications for the relations between Dermoptera and Chiroptera. Although propatagial muscles may have developed several times (*8*), there is no *a priori* reason to assume that the propatagial muscle complex would be innervated by cranial nerve VII, as evidenced by its innervation by spinal nerves 14 to 16 in birds (*14*). It is therefore more parsimonious to consider the innervation by cranial nerve VII as a shared derived character uniting all winged Archonta, as in cladogram B.

Our data confirm that Dermoptera are an appropriate structural intermediate between quadrupedal mammals and flying bats (*3, 15*) and suggest a model for the evolution of bat flight muscles. The propatagial muscle complex of Dermoptera consists of two layers of muscles, each innervated by nerves from a single source. In bats, a more complicated pattern arose: the two muscles fused and were rearranged at their origin. The originally homogeneously distributed muscle mass differentiated into a series of muscle bellies separated by tendons. The innervation of both original muscles was retained for each of the bellies, leading to the novel pattern of dual innervation. Small variations in the differentiation of the original muscle sheets led to the different arrangements characterizing Recent families of bats (*16*).

This model is consistent with the available evidence. A further test would be to study the ontogenetic trajectory of the propatagial muscle complex in Chiroptera, which may show the retention of primitive patterns of innervation.

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A Heparin-Binding Growth Factor Secreted by Macrophage-Like Cells That Is Related to EGF

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Macrophage-like U-937 cells secrete a 22-kilodalton heparin-binding growth factor that is mitogenic for BALB-3T3 fibroblasts and smooth muscle cells, but not endothelial cells. The amino acid sequence predicted from complementary DNA clones indicates that the mitogen is a new member of the epidermal growth factor (EGF) family. This heparin-binding EGF-like growth factor (HB-EGF) binds to EGF receptors on A-431 epidermoid carcinoma cells and smooth muscle cells, but is a far more potent mitogen for smooth muscle cells than is EGF. HB-EGF is also expressed in cultured human macrophages and may be involved in macrophage-mediated cellular proliferation.

MACROPHAGES HAVE A CENTRAL role in mediating the body's immune and inflammatory responses, in large part through the production of over 100 substances that influence these responses (*1*). They also produce growth modulators that have been implicated in the proliferation of connective tissue cells and the induction of angiogenesis that occurs in wound repair; these modulators include basic fibroblast growth factor (bFGF), platelet-derived growth factor (PDGF), transforming growth factor–α (TGF-α), transforming growth factor–β (TGF-β), and tumor necrosis factor–α (TNF-α) (*2*). In addition, it has been suggested that macrophages are involved in the etiology of atherosclerosis (*3*), and the smooth muscle cell hyperplasia that accompanies atherosclerosis has been attributed to PDGF, a potent smooth muscle cell mitogen produced by macrophages as well as platelets (*4*).

We used heparin-affinity chromatography, a method that greatly facilitated the purification of bFGF (*5*) and acidic FGF (*6*), to further characterize the growth factors secreted by macrophages. Initial results (*7*) indicated that cultured human macrophages

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