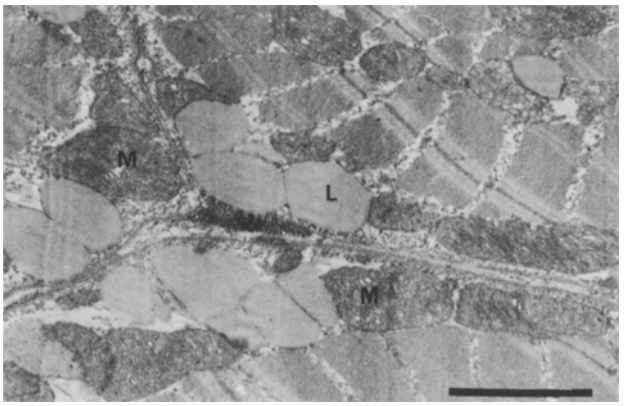
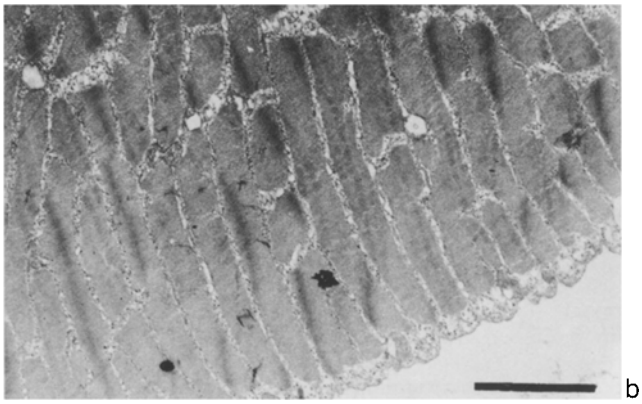


a

a White muscle. Note the few, small mitochondria and the lack of lipid. × 3070. Bar represents 5 μm.



b

b Red muscle. There are many large mitochondria (M) and lipid droplets (L). × 3700. Bar represents 5 μm.

This inability to improve the aerobic capacity is undoubtedly related to the poor blood supply of fish muscle, and this is probably a function of the low arterial blood pressure produced by passage of blood through the gills.

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Localization of substance P-immunoreactive nerve fibers in the human digital skin

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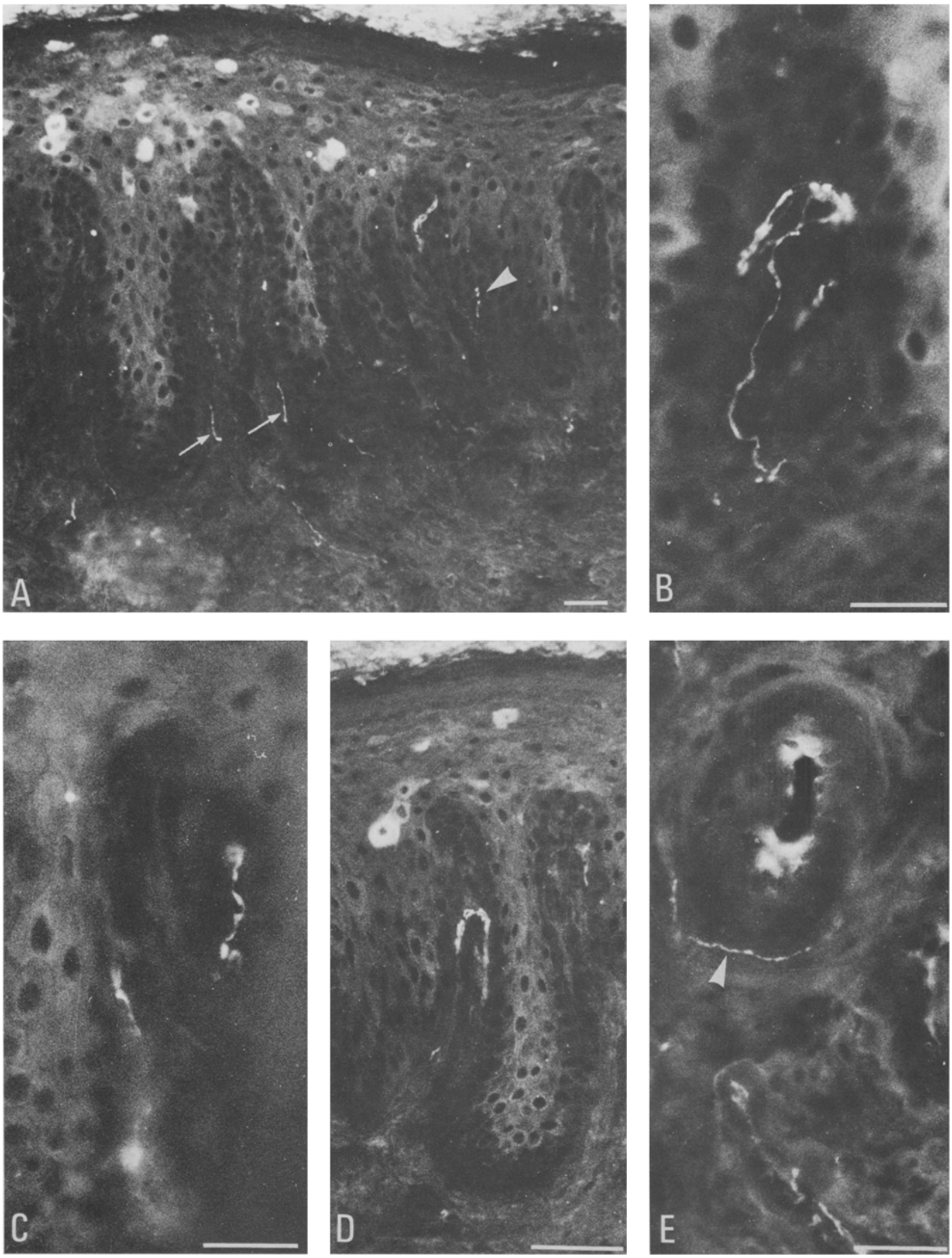
Summary. Substance P-immunoreactive nerve endings were localized in human digital skin by the use of indirect immunohistochemical technique. It was found that substance P-like immunoreactivity was present in free nerve endings in the dermal papillae and in the epidermis. Some Meissner's corpuscles also contained substance P positive nerve endings. Furthermore, substance P-immunoreactive nerves were localized in close connection to sweat gland ducts and blood vessels. The functional significance of these findings was discussed with regard to pain mediation and inflammatory response.

Substance P (SP), originally discovered by von Euler and Gaddum[2] and identified as an undecapeptide by Chang and Leeman[3] has a widespread distribution in the central and peripheral nervous system, as revealed by biochemical[4,5] and immunohistochemical[6,7] techniques. The higher concentration of SP in the dorsal roots compared to the ventral roots led Lembeck[4] to suggest that SP was a transmitter substance in the primary afferent neurons. This was strongly supported by the elegant biochemical and electrophysiological experiments of Otsuka and colleagues[8]. Immunohistochemical studies have shown SP-like immunoreactivity in a population of predominantly small sized sensory neurons with central axons terminating in the superficial laminae of the dorsal horn and spinal trigeminal nucleus and the peripheral branches innervating the skin[7,9]. Furthermore, electrophysiological studies have demonstrated an action of SP on nociceptive units in the spinal cord[10,11]. SP has also been shown to play an important role in the peripheral tissues in neurogenic inflammation, causing vasodilation and plasma extravasation by antidromic activation via axon collaterals[12].

In the present study the occurrence of SP immunoreactive fibers and nerve endings in human digital skin has been investigated, by the use of an indirect immunohistochemical technique.

Blocks of human digital skin were taken with a 3-mm punch from the palmar part of the distal phalanges of healthy volunteers (the authors). The specimens were immediately fixed in a fresh solution of 0.2% parabenzoquinone and 2% paraformaldehyde for 2 h[13,14], stored overnight in 0.1 M phosphate buffer solution with 5% sucrose added, cut perpendiculary on a cryostat at 14 μm and then processed for indirect immunohistochemistry according to Coons and collaborators[15]. Briefly, the sections were incubated in a humid atmosphere at 4 °C for 18–24 h with monoclonal antibodies to SP (dilution 1:200)[16], rinsed and incubated with FITC-conjugated rabbit anti-rat antibodies (dilution 1:10, Miles, U.K.) at 37 °C for 30 min, rinsed,



Immunofluorescence micrographs of human digital skin after incubation with SP antiserum *A* Several SP-positive fibers are seen in the deeper layers entering the dermal papillae where both free (arrows) and beaded nerve endings are observed. Arrow head points to a free nerve ending in the epidermis. *B* A dermal papilla with a SP-positive Meissner ending. *C, D* SP immunoreactive nerve endings in dermal papillae with a beaded appearance. *E* SP immunoreactive nerve fibers (arrowhead) in connection with a sweat gland duct. The fluorescent epidermal cell bodies seen in (A) and (D) and in the inner surface of the sweat gland ducts in (E) were not SP immunoreactive. Scale bar: 25 μm.

mounted and examined in a Zeiss fluorescence microscope equipped with a KP 500 excitation filter and a LP 520 stop filter. SP antiserum preabsorbed with an excess of SP (10 nmoles/ml diluted serum) was used as control serum. After photography, the cover slips were removed, and after rinsing the sections were stained with hematoxylin-eosin for identification of Meissner's corpuscles.

In the dermis and dermal papillae a large number of SP-immunoreactive nerve fibers were observed (fig., A). These fibers seemed to be of different type with regard to morphology and distribution (fig., A–D). Most of the SP positive fibers were free nerve endings in the papillae but a few could also be seen entering the epidermal layer (fig., A). In a few papillae SP-positive endings were seen in Meissner's corpuscles (fig., B), whereas other papillae contained beaded SP-positive endings in the cupular portion, without obvious association to Meissner's corpuscles (fig., C,D). In the deeper layers some SP immunoreactive nerve fibers were found in close contact to sweat gland ducts (fig., E) and in relation to blood vessels. No fluorescent nerve fibers were observed when the control serum was used. In the epidermis a population of cell bodies exhibited a green fluorescence (fig., A and D). This fluorescence was regarded as unspecific, since it occurred also on consecutive sections incubated with the control serum.

The present results give strong evidence for a SP-like peptide in free nerve endings and in Meissner's corpuscles of the human digital skin. No definite evidence for occurrence of SP-positive nerves in Merkel's discs was obtained. The distribution and morphology of the SP immunoreactive nerve endings resemble the distribution and morphology of small diameter nerve fibers described earlier by the use of light and electron microscopical techniques[17–19], and suggest that they are sensory in nature. The finding of SP-like immunoreactivity in free nerve endings in human digital skin is consistent with earlier observations in cat[7] and rat[9].

Free nerve endings have been suggested to be involved in nociception[20] in contrast to the Meissner's corpuscles, which have been associated with transmission of mechanical stimuli[20]. Thus, SP-like immunoreactivity is observed in nerve endings with apparently different physiological properties. Cauna[17] has, however, reported that a few Meissner's corpuscles contain a 2nd type of nerve endings, in addition to the large diameter fibers reacting to mechanical stimuli. These fibers were thin and resembled the free nerve endings but had a winding course, similar to that of the large diameter nerves, within the corpuscle. It was suggested that these fibers were associated with pain transmission rather than non-noxious stimuli[17]. Although the SP-immunoreactive nerve fibers in some Meissner's corpuscles most likely represent the type of nerves associated with pain mediation, it cannot be excluded that there exists a second population of SP containing sensory neurons reacting to mechanical stimuli (see also Henry[10]).

Free nerve endings within the dermal papillae were often observed in close connection with capillary loops[18]. Such arrangements may be the morphological background for the neurogenic inflammatory processes, where SP mediated vasodilatation and plasma extravasation occurs after antidromic stimulation of sensory nerves[12]. These mechanisms have been suggested to take part via axon collaterals of SP-containing primary sensory neurons[12,21].

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Studies on chemotherapy of parasitic helminths (XVII). Effects of pyrantel on the motility of various parasitic helminths and isolated host tissues

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Summary. Pyrantel tartrate caused spastic paralysis in various parasitic nematodes, but not in cestodes and trematodes.

Since Austin et al.[1] discovered the anthelminitic effects of pyrantel tartrate (pyrantel) from laboratory assays using *Nematospiroides dubius* in mice and *Nippostrongylus muris* in rats, there have been many reports regarding the in vivo efficacy of this drug in animals[1,2] and man[3,4]. It was reported that pyrantel is effective against various intestinal