lumens of the capillaries and venules. Where the capillaries were close to the arterioles, there were few fenestrae and the particles were relatively rare near the vessels and in their lumens. The venous limbs of the capillaries had many fenestrae and the particles were plentiful both adjacent to the vessels and in their lumens. The differences in the distributions of the particles, near the vessels and in their lumens, is consistent with their being swept towards and into the venous limbs by the extravascular fluid passing from the arterial to the venous ends of the capillaries in accordance with Starling's hypothesis. (In mammals the much larger chylomicra similarly accumulate around the lacteals[15].) While it is impossible to say with certainty, it would seem, from the apparent ease with which the particles enter the capillaries, that most of them pass via the fenestrae rather than via the slow system of small vesicles[8–10]. (Generally the vesicles cannot provide a net removal of extravascular proteins because the concentrations of these in most of the body are lower than those in the blood[8, 10].)

In the ciliary body the fenestrae were much more frequent in the capillaries in the ciliary process than in those in the muscle. The capillaries in the process are close to the veins; those in the muscle are close to the arteries. Hence it appears that there also, as in the gut[2], the adrenal[4], the rete of the renal medulla[16] and the swim bladder[17], and the skin[7], fenestrae are concentrated on the venous limbs of capillaries. This, together with their possession of diaphragms, are likely to be of fundamental importance for their uptake of large molecules from the tissues[2–4].

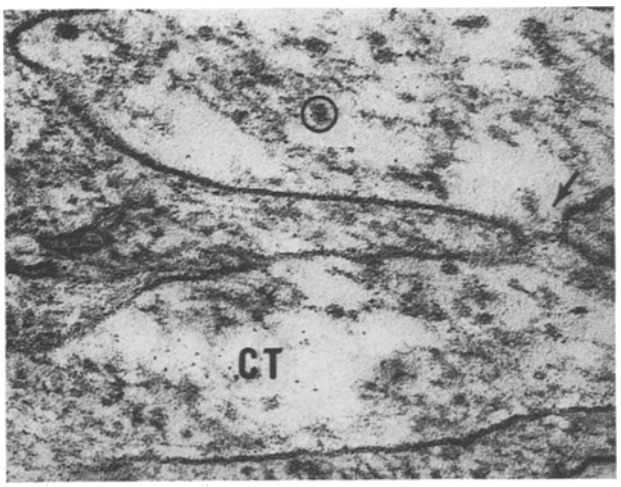

Fig. 3. Venous limb of a capillary in an intestinal villus. There are numerous particles (circles) which resemble lipoproteins as seen in mammals. They are present in the connective tissue (CT) and lumen. One is very close to a fenestra (arrow). × 100,000.

Since *Heterodontus* has fenestrae but no true lymphatics, it seems conclusive that fenestrae antedate the lymphatic system. It also appears that they allow large molecules to enter the blood capillaries on their venous limbs[3]. We are left, then, with the problem of why the lymphatic system developed and what its important functions are.

In some regions the lymphatics are indubitably important for the clearance of particles and large molecules, particularly those larger than the fenestrae. E.g. in the skeletal muscle and in all the regions of the body where fenestrae are infrequent, especially bordering mesothelium lined cavities. It is likely that they are still of importance, even in the presence of fenestrae, if there is much lymph flow, e.g. in the villi of the mammalian gut during digestion. However, they are by not means essential for the uptake of large molecules.

DRINKER[18] suggested that the lymphatics function primarily as spillways to remove the large accumulations of extravascular fluid which occur in active muscles. It may be that the lymphatics developed for this reason in the higher fish, with their higher blood pressures. Then they could also remove large molecules during periods of high lymph flow[19].

Résumé. Le requin n'a pas de vrais vaisseaux lymphatiques, mais ses capillaires sanguins sont fénestrés. On suppose que les grandes molécules sont éliminées des tissus par ces fenestrae.

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Depolarization of Tooth Pulp Primary Afferent Fibers in the Medulla oblongata

The depolarization of primary afferent fiber terminals in the spinal cord and medulla oblongata has been the subject of intensive investigation, and evidence has accumulated to show that it is causally related to pre-synaptic inhibition[1, 2]. Depolarization of fast-conducting cutaneous fibers can be produced by stimulation of other fibers belonging to the same afferent group[3].

The aim of this study was to see whether an analogous presynaptic control mechanism exists at central terminals of the afferent fibers supplying the tooth pulp. These fibers consist of slow-conducting fibers with maximum velocity 30–45 m/sec[4] and it is generally recognized that pain is the only modality of perception they subserve[5].

Material and methods. The experiments were carried out on 16 cats anesthetized with Nembutal. Animals were fixed in a stereotaxic holder, the posterior fossa was exposed and part of the cerebellum removed to gain access to the medulla oblongata. The infraorbital nerve was exposed and a bipolar stimulating electrode placed close to its point of exit from the infraorbital foramen. Two cavities were then prepared in the upper and lower canine teeth and filled with Ringer agar gel. Tungsten wire

electrodes inserted in the cavities could be used for either stimulating or recording[6]. The animals were immobilized with Flaxedil and artificially respired. The excitability changes of the terminals of the tooth pulp afferent fibers in the medulla oblongata were determined by the technique of WALL[7] which is schematically depicted in Figure 1, A.

Results and discussion. A glass capillary microelectrode filled with 4 *M* NaCl was inserted into the nucleus of the spinal trigeminal tract to such a depth that large negative field potentials were recorded upon stimulation of the infraorbital nerve and stimulation of the afferent nerve fibers in the tooth pulp (Figure 1, B). Field potentials produced by stimulating lower or upper canine were found to be restricted to the oral part of the nucleus tractus spinalis n. trigemini[8]. The stimulating and recording positions were then reversed and cathodal rectangular pulses were applied to the microelectrode in the nucleus at a strength adequate to give submaximal responses recorded antidromically from the tooth (Figure 1, C). Increased excitability of the tooth's primary afferent terminals was observed when the antidromic action potentials recorded in the periphery were preceded by a conditioning orthodromic volley in the infraorbital nerve. This is shown in the upper traces in Figure 1, D–F, for 3 selected intervals. Antidromic potentials were of a complex configuration and therefore quantitative estimation of excitability changes was made by comparing planimetrically determined areas enclosed by the antidromic potential between the time limits indicated in Figure 1, D. The time course of increased excitability of the tooth pulp primary afferent terminals exhibits a steeply rising phase with the maximum increase of excitability being reached after about 20 msec. The descending phase is prolonged and returns to the base line in about 200 msec. Thus, the time course of the increased excitability of delta tooth primary afferent fibers resembles that of the fast conducting fibers in other trigeminal cutaneous branches[2].

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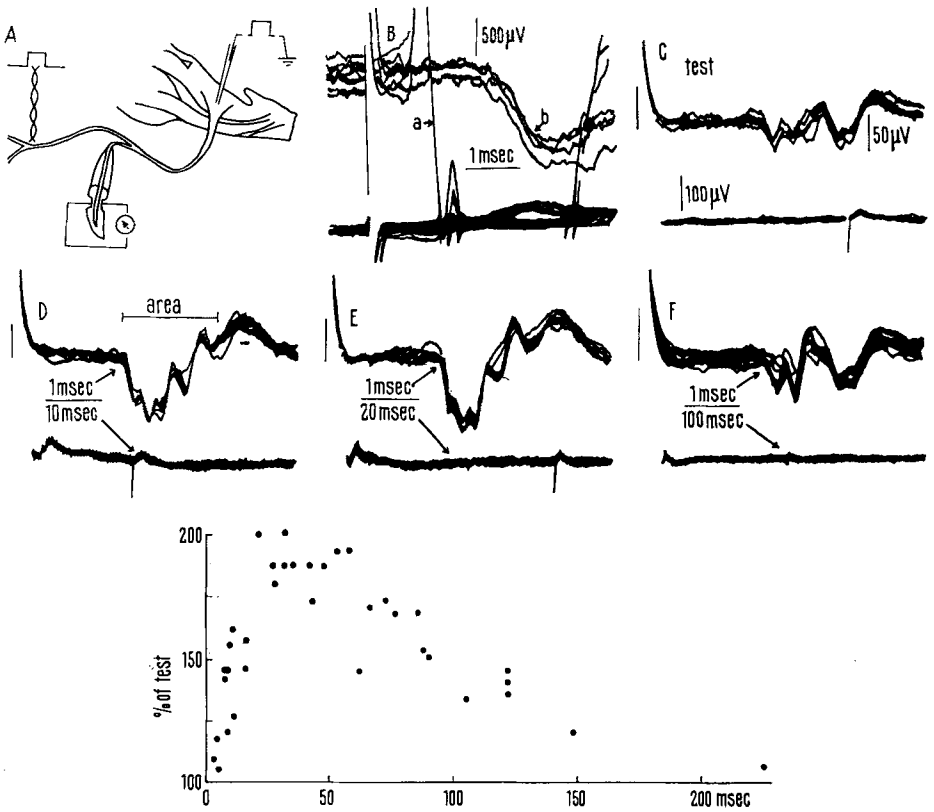

Fig. 1. Excitability changes of the tooth pulp afferent fibers evoked by stimulation of the infraorbital nerve: (A) Experimental arrangement. (B) Field potentials recorded by a 4 *M* NaCl capillary microelectrode inserted into the rostral part of the spinal trigeminal nucleus 7 mm above the obex, on stimulation of the infraorbital nerve (a) and the upper cannine (b). Lower traces, as in all recordings, are monopolar recordings from the surface of the medulla 3 mm below the obex. (C) Antidromic action potential recorded from the upper canine, evoked by submaximal shock applied to the microelectrode inserted at the place of maximal field potential as shown in (B). (D–F) The increase of the antidromic action potential produced by a preceding volley in the infraorbital nerve at 3 different time intervals. The interval between conditioning and test stimulus is seen on the lower recordings taken at slower speeds. The limits of the planimetric measurement of the area confined by the complex antidromic potential are indicated by the horizontal bar in (D). The graph shows the time course of the increased excitability expressed as percentages of the antidromic action potential following a stimulus applied to the infraorbital nerve at intervals indicated on the abscissa.

The relative effect of impulses in the low and high threshold afferent fibers on the excitability changes in the tooth primary afferent terminals was examined by varying the strength of the conditioning stimuli applied to the infraorbital nerve and by stimulating the δ fibers of another tooth pulp. The threshold for the infraorbital nerve was estimated from responses recorded by a monopolar electrode placed on the surface of the medulla 3 mm below the obex. Increased excitability was already apparent when the strength of conditioning stimulus was 1.2 × treshold and it increased rapidly, reaching approximately 90% of its maximum at the 5 × threshold strength. Figure 2, B shows the optimum interval of the increased excitability of the tooth pulp primary afferent terminals produced by a conditioning volley in the infraorbital nerve at 3.7 × threshold. When conditioning stimuli were applied to the tooth pulp of the other ipsilateral canine tooth a similar increase in the antidromic potential evoked by the test shock was seen. This is shown by Figure 2, D only for the optimum interval, but the time course and magnitude of changes of the excitability were similar to that observed after a preceding volley to the infraorbital nerve. It can, therefore, be concluded that impulses in both fast-conducting A α- and β-fibers as well as slow-conducting A δ fibers contribute to the depolarization of tooth pulp primary afferent terminals in the medulla oblongata[9].

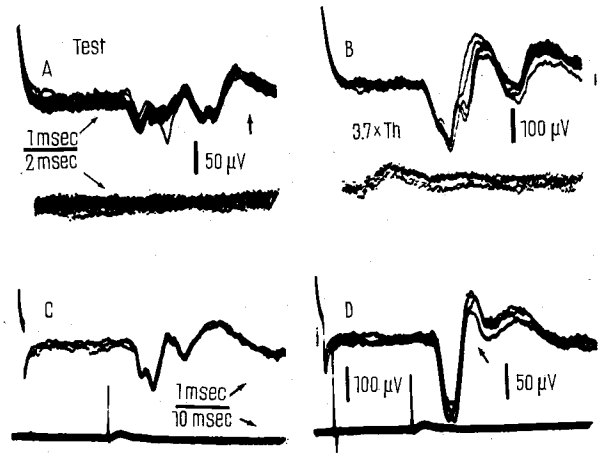

Fig. 2. (A–B) Excitability changes of the tooth pulp primary afferent terminals evoked by an impulse in low threshold trigeminal afferent fibres. Upper traces, antidromic action potentials recorded from the upper canine; lower traces, monopolar recordings from the surface of the oblongata 3 mm below obex. (A) Control, (B) the same preceded in the interval of 20 msec by a stimulus to a branch of the infraorbital nerve at a strength 3.7 times threshold. (C–D) Excitability changes of the tooth pulp afferent terminals evoked by an impulse in δ fibres of another tooth. Upper traces, antidromic action potential from the tooth pulp of the upper canine; lower traces, monopolar recordings from the surface of the oblongata at lower speed. (C) Control, (D) the same preceded by a volley in the tooth pulp of lower canine.

Zusammenfassung. Die zentralen Endigungen der primären afferenten Fasern der Zahnpulpa, welche ausschliesslich der A-δ-Gruppe angehören, können sowohl durch Impulse in A-α-und β-Trigeminus-Fasern als auch in A δ afferenten Fasern der Pulpa eines anderen Zahnes depolarisiert werden.

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Spontaneous Sympathetic Activity in Experimental Heart-Failure

The marked decrease in catecholamine levels in clinical and experimentally produced congestive heart failure (CHF) is a well-documented finding[1–3]. The exact mechanism whereby the noradrenaline content is reduced in the sympathetic nerve terminals at the heart is not completely understood. It has been suggested[4] that the defect lies in the synthesis or binding of norepinephrine. CHIDSEY and BRAUNWALD[1] later presented evidence which supported the view that depletion of cardiac norepinephrine was a consequence of a reduction in the number of nerve endings. It has also been reported[5] that postganglionic sympathetic nerve stimulation elicits a reduced cardiac response in dogs with experimentally produced heart-failure. Cardiac muscle from cats in experimental heart-failure has been shown to be in a depressed contractile state[7]. SIEGEL and SONNENBLICK[6] suggested that animals in CHF may maintain or increase their cardiac contractility by an increase in the spontaneous sympathetic activity due to vasomotor reflex mechanisms. Pharmacological evidence has been presented[1] which suggests that there is an increased sympathetic nervous discharge in patients with heart-failure. In this study we directly measured spontaneous sympathetic nerve activity to the normal and failing heart in order to determine whether the failing heart is supported to any degree by increased sympathetic activity.

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