

β -adrenergic receptors of the frog heart could be modified under certain experimental or physiological conditions. In earlier reports from our laboratory¹⁴⁻¹⁹, we have pointed out that the NE uptake system in cold blood animals differs in some aspects from that in hot blood species. In order to discard the possibility that this fact was dependent upon the blood temperature, we carried out a series of experiments with isolated atrium of guinea-pig. The results obtained showed that LiCl produces a positive inotropic response per se that immediately falls to a control value. The possibility that this positive inotropic response could be due to an immediate release of endogenous NE produced by lithium was discarded in a series of experiments with reserpinized animals in all of which appeared this response (Figure 1). We do not believe that the competitive antagonism potassium-lithium described by PLOEGER and DEN HERTO²⁰ could be responsible for this response. The hypertonicity of the incubation medium could be a factor to take into account but in control preparations with a hypertonic Krebs (with

NaCl) the inotropic positive response did not appear; on the contrary, an inotropic negative response is produced which is immediately restored to normal values (Figure 1). On the other hand, the sensitivity to NE is smaller in LiCl-treated preparations in comparison with controls treated with an excess of sodium, and maximal response to NE was not obtained in any of the LiCl-treated experiments (Figure 2).

These results support the idea that in this sense lithium has 2 different effects on the sympathetic nerve endings of the heart; 1. a neuronal action with a blockade of the catecholamine uptake (uptake 1) and 2. an extra-neuronal action with a great decrease in the sensitivity of the β -adrenergic receptor. This could be the reason why the cocaine-like effect not appear. On the other hand, the treatment with tyramine after incubation with NE does not produce a positive inotropic response in lithium-treated preparations (Figure 3). This could be explained if we assume that lithium not only blocks the NE uptake but also blocks the transfer site of tyramine across the neuronal membrane. Further investigations are being carried out in our laboratory in order to reach a satisfactory conclusion.

Resumen. El cloruro de litio se comporta como bloqueante de la incorporación de H³NE al ventrículo aislado de *Rana*. En aurícula aislada de cobayo el cloruro de litio produce efecto inotrópico positivo per se y aumenta el umbral de excitabilidad a la NE administrada exógenamente.

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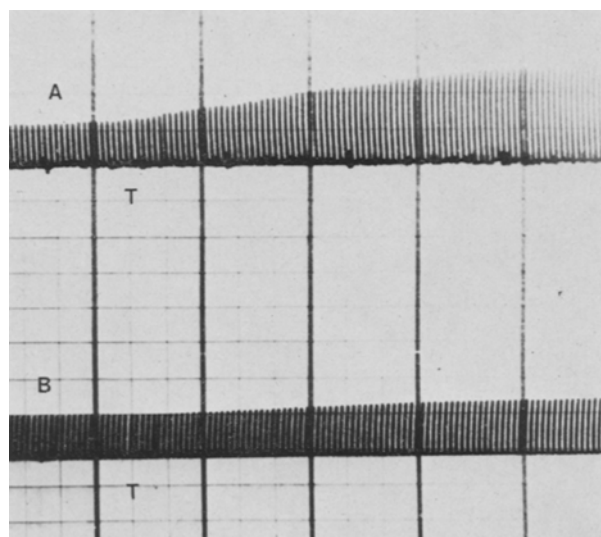


Fig. 3. Isometric contraction from stimulated left atrial preparation obtained from a reserpine-treated guinea-pig after incubation with norepinephrine. A positive inotropic response to tyramine (T) appeared only in the control preparation. B) Experimental half: normal Krebs plus 100 mM of lithium chloride. A) Control half: normal Krebs plus equimolar amounts of sodium chloride. T, 10^{-6} g/ml of tyramine.

Types of Cell Contacts in Arterial Smooth Muscle

Some form of close contacts occurs between smooth muscle cells of arterial blood vessels. These have often been designated as nexuses or gap junctions^{1,2}, though the characteristic five-layered appearance of gap junctions seen after the usual fixation and double staining procedure has been demonstrated only in larger vessels³⁻⁷. Since it is now recognized that several types of cell junctions may occur in various kinds of smooth muscle⁸ and that gap junctions are absent from at least one kind which exhibits cell-to-cell electrical coupling^{8,9}, it is of interest to examine which types of contacts may be involved in electrical coupling in arteries and terminal arterioles.

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Canine duodenum was fixed by intra-arterial perfusion with Krebs-Ringer solution containing 1.18% glutaraldehyde⁹, rabbit aorta and carotid artery by immersion in 5% glutaraldehyde in Millonig's phosphate buffer. Tissues were then postfixed in 1% osmium tetroxide, dehydrated in a series of ethanols, and embedded in Epon. After staining, sections were viewed with a JEM-7A electron microscope.

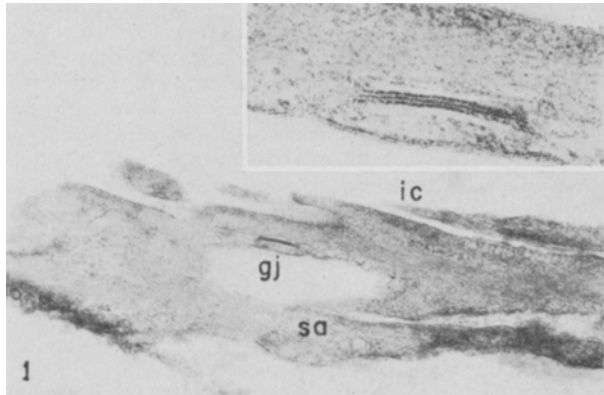


Fig. 1. Three types of cell contact in rabbit carotid artery. sa, simple apposition; gj, gap junction or nexus; ic, intermediate contact. $\times 20,000$. Inset: higher magnification of gap junction, showing five-layered structure. $\times 100,000$.

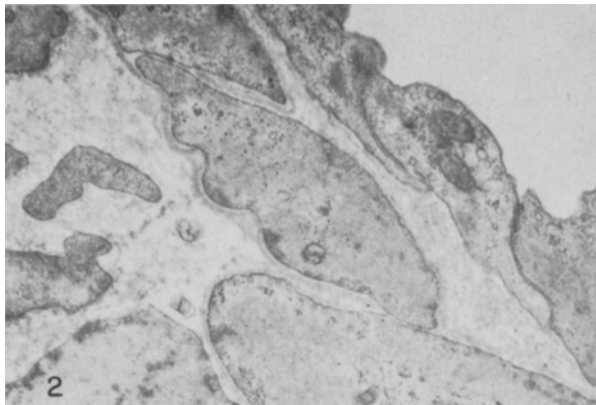


Fig. 2. Canine duodenum, terminal arteriole. Simple appositions between smooth muscle cells, at either end of lateral intercellular space. $\times 20,000$.

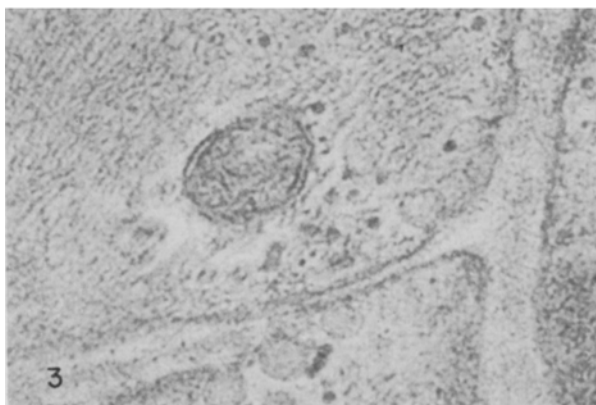


Fig. 3. Simple apposition in terminal arteriole, showing lack of specialization of cytoplasm or plasma membrane at this point. $\times 80,000$.

The most common type of junction between smooth muscle cells of aorta and carotid artery was found to be a simple apposition, with a clear separation of 10 nm or less between cells (Figure 1). The basement membrane is absent at this point, and there is no evidence of membrane or cytoplasmic specialization. Rarely, a typical five-layered gap junction was observed, as were regions of wider but parallel cell separation with increased membrane density and a central dense line (Figure 1). The latter have termed 'intermediate contacts' in longitudinal muscle of the small intestine, where they appear to be the only type of contact present⁹.

In terminal arterioles of the duodenum, close contacts were observed, located at the endothelial and/or adventitial ends of the lateral intercellular spaces (Figures 2 and 3). The contacts resemble the simple appositions of larger vessels. In contrast, gap junctions were frequently demonstrated in the adjacent circular muscle of the intestine of the same section (Figures 4 and 5). Gap junctions were not seen in arterioles, though certain arterioles are known to be electrically coupled².

Gap junctions or nexuses can be clearly distinguished from simple appositions, even at moderately low magnification. Gap junctions have a dense appearance against the relatively clear adjacent cytoplasm in contrast to the clear cell separation and lack of local specialization of simple appositions. In addition, mitochondria, or more frequently the glycogen particles associated with mito-

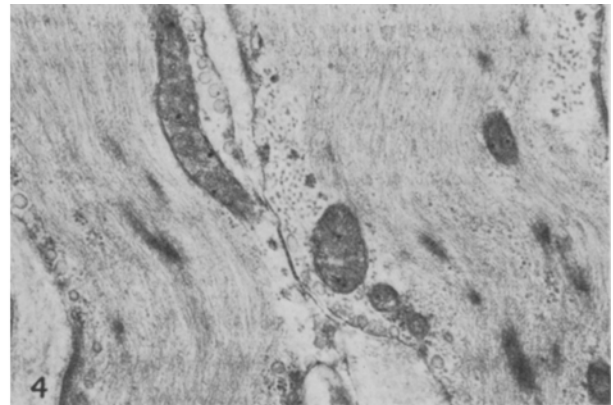


Fig. 4. Canine duodenum, circular muscle. Gap junction, with clear areas of cytoplasm on either side, and adjacent mitochondrion and glycogen particles. Same tissue section as Figure 2. $\times 20,000$.



Fig. 5. Gap junction in circular muscle, showing five-layered appearance, mitochondrion, and glycogen. Same tissue section as Figure 3. $\times 80,000$.

chondria, are usually present near gap junctions but not near simple appositions. The fact that the two distinct types of junctions occur within the same blood vessel, or in two different kinds of smooth muscle within the same tissue sections, argues against the possibility that they represent the same type of contact which has been altered by conditions of fixation. Presumably, simple

appositions, the only contacts present in terminal arterioles, are involved in cell-to-cell propagation of activity¹⁰.

Zusammenfassung. Nachweis, dass in Arteriolen sowie in präkapillaren Arteriolen des Hunde-Duodenums nur eine einfache Aneinanderlagerung der Muskelzellen erfolgt und keine «gap junctions», wie sie in den Muskelschichten der Hohlwandorgane vorhanden sind.

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Septate-Like Junctions Between Spermatogonia in Human Seminiferous Epithelium

Since the first description of septate desmosomes between adjacent epithelial cells of the Hydra by WOOD¹, septate junctions have been found between various epithelial cells of invertebrates²⁻¹¹. From studies on sections tangential to the plasma membrane, it has become evident that the septa form a well defined hexagonal network. The functional significance of these junctions is not fully understood. They were initially thought to be the only sites of low electrical resistance^{12,13}. But recent reports have indicated that macular gap junctions, which have been implicated in low resistance coupling of vertebrate tissues, can also be found along with septate junctions in invertebrate epithelia^{8-10,14-16}.

Although septate junctions were originally thought to be a unique feature of invertebrate epithelial cells, they have now been reported in several vertebrate tissues. LASANSKY et al.¹⁷ found them at synaptic endings of the turtle visual cells, GOBEL¹⁸ in the basket formation of the cat cerebellar cortex, and SOTELO and LLINAS¹⁹ in the cerebellar cortex of rats and cats. The morphological features of the junctions between neuronal elements of vertebrates closely resemble those described for invertebrates. Yet, there are some differences with regard to their length and frequency of occurrence. The well documented septate junctions between cells of the rat adrenal cortex reported by FRIEND and GILULA²⁰ seem to

be real structures, although they differ from the septate desmosomes of invertebrates with regard to periodicity and structure of the septa.

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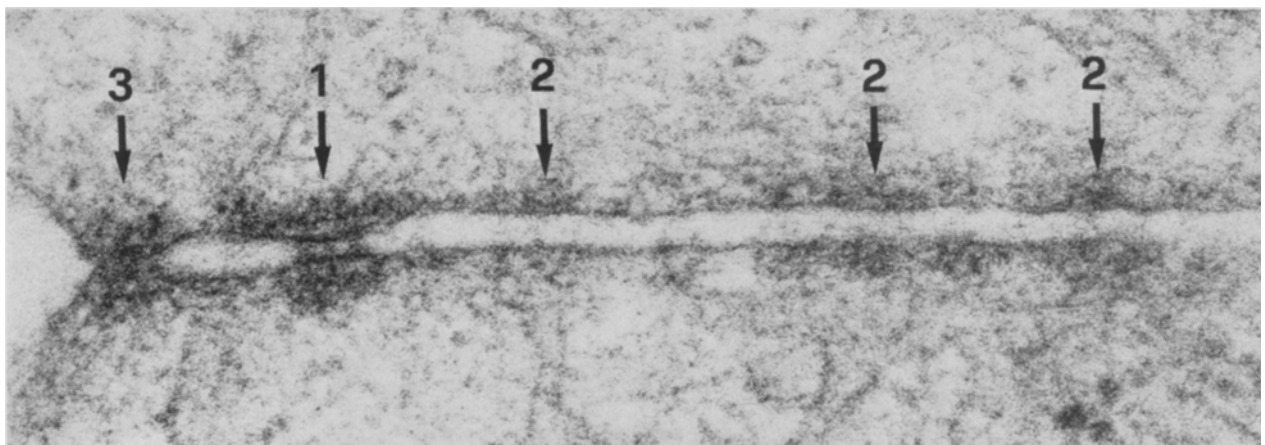


Fig. 1. Electron micrograph showing a contact area between 2 type A spermatogonia in a patient with impaired fertility. At 1 the intercellular space is narrowed and bridged by 3 septa. The apposed plasma membranes are densified, and subjacent to them condensations of cytoplasmic material are evident. The numbers 2 indicate other accumulations of cytoplasmic material and vague intercellular structures. At 3 an undetermined contact area is seen. $\times 150,000$.