section and cervical ganglionectomy. In preliminary experiments, administration of phentolamine (1–3 mg) antagonizes the venoconstrictive effects of both norepinephrine and bradykinin. It is suggested that the primary vascular event subsequent to bradykinin administration is venoconstriction. Secondarily, capillaries may be dilated passively by the pressure increase resulting from momentarily-impeded flow. (Supported by a grant from the Louisiana Heart Association.)

17. Enzymatic Kinin Release from Purified Kininogen and from Low Molecular Compounds. E. HABERMANN (*Institut für Pharmakologie und Toxikologie der Universität, Würzburg, Germany*).

The kinins released from bovine kininogen by highly purified enzymes (kallikreins, trypsin, crotalus venom) have been identified by a combination of column chromatography and biological testing. Two types can be distinguished: kinin-9-forming enzymes split kinin-11 (met-lys-bradykinin) and bradykinyl–serine bond besides kininogen. For the kinin-10-forming pancreatic kallikrein, only kininogen serves as substrate. Pig serum kallikrein belongs to the former group of enzymes. The purification and some of the pharmacological and biochemical characteristics of swine serum kallikrein will be described. For a closer approach to the portion of kininogen that can be activated, peptic fragments of the purified protein have been fractionated by a combination of chromatographic procedures. Two kinin-yielding peptides have been isolated, their structure determined, and their reaction products with kinin-forming enzyme identified. Both peptide fractions as well as further peptic fragments derived from kininogen are active on rat uterus, guinea pig ileum, rabbit blood pressure, and capillary permeability; therefore, 'pepsitocin' is a term which covers various kinins.

18. Effects of Bradykinin and Angiotensin on Ganglionic Transmission. W. HAEFELY, A. HÜRLIMANN and H. THOENEN (*Dept. of Experimental Medicine, Hoffmann-LaRoche, Inc., Basle, Switzerland*).

The effects of bradykinin and angiotensin on synaptic transmission were studied in the superior cervical ganglion of the cat. Both polypeptides produced an inhibition of ganglionic transmission in extremely low doses. For close-arterial injection to the ganglion, threshold doses were of the order of 10^{-18} moles for angiotensin. Bradykinin was slightly less potent on a molar basis and the inhibition of transmission less pronounced. A peculiar dose–effect relationship was observed regularly with both polypeptides, two ranges of effective doses being separated by a wide dose range within which no effect on ganglionic transmission occurred. Interaction of bradykinin with other drugs at the ganglionic level will be reported and possible mechanisms of the action on ganglionic transmission discussed.

19. Bradykinin and Pulmonary Vascular Permeability in Isolated Blood-Perfused Rabbit Lungs. A. HAUGE, P. K. M. LUNDE and B. A. WAALER (*Institute of Physiology, Univ. of Oslo, Norway*).

Bradykinin has been found to cause vasodilation in most areas of the systemic circulation, where another reported effect is increased capillary permeability. In the pulmonary vascular bed of various species, however, bradykinin seems to cause vasoconstriction.[1–4] We have tried to evaluate the possible effect of bradykinin on vascular permeability in isolated rabbit lungs, perfused with homologous heparinized blood at constant-volume inflow (average flow 234 ml/min). The weight of the preparation, the inflow pressure, and the tidal air were followed continuously.

When infusions into the pulmonary artery of 6 to 200 μg synthetic bradykinin per min were started or stopped, rapid weight changes were observed. These changes were apparently related to the vasoconstriction caused, and they were interpreted as being due to capacity changes in the vascular bed. No weight changes indicating alterations in net fluid movement across the vascular wall could be observed during infusions. Bradykinin infusions were also carried out during periods with elevated left atrial pressure and during reversed perfusion (left atrial inflow), both situations giving a high pulmonary capillary pressure with steady net outward filtration of fluid. Bradykinin infusions under such conditions did not influence the steady weight increase of the preparation.

It is concluded that intravascularly-infused bradykinin in doses large enough to give marked vasoconstrictor responses does not increase vascular permeability in the pulmonary vascular bed of rabbit lungs. The vasoconstriction caused must mainly occur at precapillary sites.

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20. Further Experiments on the Role of Plasma Kinins as Mediators of Functional Vasodilatation in Glandular Tissues. S. M. HILTON (*Dept. of*

Physiology, The Medical School, Birmingham, England).

In many glandular tissues which display intermittent secretory activity, this function is accompanied by a local dilatation of the arterioles, which permits a great increase of blood flow through the tissue or organ concerned. It is ten years since the hypothesis was advanced that the vasodilatation is directly caused by bradykinin, or some similar plasma kinin, formed in the interstitial fluid of the gland as a result of its activity.

The hypothesis was first formulated on the basis of experiments on the submandibular salivary gland of the cat. It has since been found to be applicable to the pancreas in the cat and to the sweat glands in man.

The recent experimental findings have enabled several possible arguments against the hypothesis to be overcome.

21. Studies of the Structure of Kininogen of Beef Serum; The Isolation of a Kinin-like Substance from the Sera of Birds. K. HOCHSTRASSER, H. SCHELLER and E. WERLE (*Klinish-Chemisches Institut an der Chirurgischen Klinik der Universität, Munich, Germany*).

The digestion of fractionated kininogen of beef serum with pepsin yields a mixture of polypeptides which contains peptides with the amino acid sequence of kinins. The peptides, which still react with kininogenases, are isolated and analyzed for amino acid composition.

Besides these polypeptides there are at least two more pharmacologically active peptides in the pepsin digest of beef serum. One lowers the blood pressure, the other raises it. Both polypeptides have been isolated, and their amino acid composition is currently under study.

Kallikrein from the pancreas of birds liberates kinin only from avian but not from mammalian serum. This kallikrein, the spontaneously formed kinin, and the kinin liberated by kallikrein from avian serum have been characterized.

22. The Action of Hypotensive Polypeptides on the Pulmonary Arterial Pressure. H. KONZETT (*Institute of Pharmacology, Univ. of Innsbruck, Austria*).

Bradykinin, kallidin, and eledoisin cause a rise of pressure in the pulmonary artery of some species. These polypeptides also contract the isolated pulmonary arteries of the same species. Under certain conditions, antiphlogistic substances antagonize the effect of bradykinin and kallidin on the pulmonary vessels *in vitro* and *in vivo*. The effect of eledoisin on these vessels is less easily antagonized by such compounds.

According to investigations on the left and right atrial pressure and on the heart–lung preparation, the increase in the pressure in the pulmonary artery after bradykinin, kallidin, and eledoisin is due, predominantly, to a direct action on the pulmonary vessels.

23. Effect of Bradykinin on Submandibular Salivary Gland Permeability. D. C. KROEGER and W. KRIVOY (*Dental Branch, Univ. of Texas and Baylor Univ. College of Medicine, Houston, Texas, U.S.A.*).

Previous investigations from these and other laboratories have demonstrated that the nerve-induced release of a plasma kinin in glandular tissue results in vasodilatation. Other studies on the central nervous system and muscles suggest that the plasma kinin, bradykinin, alters cellular permeability. The technique of Martin and Burgen (*J. gen. Physiol.* **46**, 225, 1962), using sucrose, was employed here to study the possibility that bradykinin might influence glandular permeability in addition to the aforementioned glandular vascularity. Intravenous doses of synthetic bradykinin (1–2 μg/kg) were equipotent to epinephrine (3–5 μg/kg) in causing an increase in the permeability of the dog's submandibular salivary gland to sucrose. The time courses of this response to both drugs at this dose level were similar. Phenoxybenzamine (5 mg/kg) was found to block the action of epinephrine on permeability, whereas it intensified the degree and duration of the effect of bradykinin upon the permeability to sucrose. In summary, bradykinin increases the permeability of the dog's submandibular salivary gland to a large carbohydrate molecule. This action of bradykinin appears to be independent of epinephrine. (This research was supported by funds from Grant DE01390 of the U.S. Public Health Service.)

24. Extraction of Substance P from Brain. F. LEMBECK, H. HEIZMANN and G. SEIDEL (*Pharmakologisches Institut der Universität, Tübingen, Germany*).

Substance P was extracted from pig brain by a new method. The tissue was homogenized with chloroform:methanol (2:1), centrifuged, and re-extracted; the chloroform–methanol extract, after washing with distilled water, was concentrated *in vacuo* and freeze-dried. The white powder obtained was boiled in 0·1 N HCl, and a large amount of sediment was separated. The supernatant fluid contained a substance that contracted smooth muscle. Further purification was achieved by acetic acid–ether precipitation.

This extract was compared with substance P obtained from the same tissue by the usual Gaddum-Euler method followed by acetic acid–ether precipitation. The activity ratio of both