After intravenous injections, physalaemin was only one to six times more active than eledoisin, but after intra-arterial administration it had a much stronger local vasodilating action, particularly when the basal vascular tone was high.

Eledoisin had a powerful vasodilating action on the innervated and acutely denervated vessels supplying the gastrocnemius-plantaris muscle of the dog. Denervation enhanced the peripheral vasodilating activity of vasodilatory drugs.

In the rabbit both physalaemin and eledoisin reduced systemic blood pressure and contracted the uterus *in situ*. Physalaemin was more active on blood pressure and less active than eledoisin on the uterine muscle. Moreover, its oxytocic effect was generally shorter and sometimes irregular.

On the isolated vas deferens of the guinea pig, physalaemin and eledoisin potentiated contractions caused by electrical stimulation of the hypogastric nerve, both showing a direct action on the muscle when higher concentrations were used in the bath.

14. Pharmacologically Active Peptides in Trypanosome Infections. L. G. GOODWIN (*Nuffield Institute of Comparative Medicine, London, England*).

Mice inoculated with a strain of *Trypanosoma brucei*, which causes an acute infection, excrete histamine and pharmacologically active peptide in the urine. Increased histamine and kinin activity is also found in plasma and tissues, especially skin, ears, and feet.[1, 2] Treatment with a trypanocidal drug causes a reduction in active peptide output: if the infection relapses the peptide reappears. Studies are now in progress on chronic trypanosomiasis. Rabbits infected with *T. brucei* show few organisms in the circulating blood but usually die in 30 or more days. Active peptide excretion in the urine occurs in a series of diminishing peaks, which may perhaps be related to the emergence of antigenic variants of the parasite during the course of the infection (Boreham, unpublished). Studies are also being made on the mast cells in tissues which show increased histamine and peptide content during infection.

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15. The Role of Cathepsins in the Iniactivaton of Plasma Kinins. LOWELL M. GREENBAUM and KEIKO YAMAFUJI (*Dept. of Pharmacology, College of Physicians and Surgeons, Columbia Univ., New York, N.Y., U.S.A.*).

The possibility that intracellular proteinases (cathepsins) may play a role in the inactivation of kallidin, bradykinin, and related kinins is being investigated. Evidence has been presented (*Life Sci.* **4**, 625, 1965; *Fed. Proc.* **24**, 1965) that catheptic carboxypeptidase B from spleen inactivates bradykinin *in vitro* by cleaving the COOH-terminal arginine from the polypeptide. This enzyme has now been found in liver and kidney. The enzyme has an absolute requirement for SH activators such as cysteine and mercaptoethanol. The enzyme is active optimally at acid pH. Iodoacetic acid inhibits the reaction. Free phenylalanine is also found in the reaction mixture and results from the action of catheptic carboxypeptidase A (*J. biol. Chem.* **237**, 1082, 1962) on the COOH-terminal phenylalanine produced after cleavage of the arginine residue from bradykinin by catheptic carboxypeptidase B.

The catheptic carboxypeptidase B enzyme differs from carboxypeptidase N of plasma (Erdös *et al.*, *Biochem. Pharmacol.* **11**, 585, 1962) and the carboxypeptidases of brain tissue (Krivoy and Kroeger, *Brit. J. Pharmacol.* **22**, 329, 1964) in its pH optima and requirement for SH activators. Since the possibility exists that intracellular proteinases play a role after cellular injury in the production and degradation of plasma kinins, the degradative role of the carboxypeptidases is of interest. The possible role of other catheptic enzymes in producing kinins will be discussed. (Supported by Grants AM-09393, and General Research Support, U.S. Public Health Service; and a grant from the Life Insurance Medical Research Fund.)

16. Vasoconstriction Induced by Bradykinin in the Intact Rabbit Ear (cinematographic presentation). P. S. GUTH, R. BOBBIN, G. CANO and J. AMARO (*Dept. of Pharmacology, Tulane Univ., New Orleans, La., U.S.A.*).

In a previous article (*Ann. N.Y. Acad. Sci.* **104**, 69, 1963) it was reported that bradykinin induced a constriction of veins in the intact rabbit ear as well as a decrease in outflow in preparations of the isolated rabbit ear, dog and cat hind limbs, and rat hindquarters perfused with appropriate saline solutions. The present report confirms that work and extends it.

The bradykinin-induced venoconstriction may be demonstrated in the ears of rabbits lightly anesthetized with urethane (1 g/kg i.p.). Bradykinin in doses of 2·4–4 μg, injected i.v. (via cannula in a primary branch of the marginal ear vein) in an orthodromic direction in the ear being photographed, causes constriction of the marginal vein. The constriction occurs in less than 10 sec after injection and reaches a maximum in 25–35 sec. The maximal effect thus elicited is a 50% reduction in vessel diameter.

The venoconstrictive effect of bradykinin is still present in animals with greater auricular nerve

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*