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

extracts on isolated organs (guinea pig ileum, rat uterus, hen rectal caecum, rabbit jejunum) and on rabbit blood pressure was the same in each case. The activity of both preparations was destroyed by trypsin. After separation on Al_2O_3 columns, both preparations consisted of Zetler's fraction F_a. The Euler-Gaddum extract contained in addition a small amount of F_b. Some differences between the extracts could be found after separation in paper chromatography and electrophoresis.

Four regions of the brain containing different amounts of substance P were extracted with both methods; the activity ratios between the regions were the same with each method. After the extraction with chloroform–methanol, no substance P activity remained in the tissue.

Separation of the chloroform–methanol extract by lipid extraction methods shows that the activity goes with the phosphatide fraction. From these experiments it is concluded that substance P in the brain tissue is bound to phosphatides.

25. Plasma Kinins and the Sympathetic Nervous System. GRAHAM P. LEWIS (*CIBA Laboratories, Horsham, Sussex, England*).

No abstract received.

26. The Influence of Substitution or Omission of an Amino Group on the Hypotensive Activity of the C-Terminal Sequences of Eledoisin. K. LÜBKE and E. SCHRÖDER (*Schering AG, Hauptlaboratorium, West Berlin, Germany*).

Most of the analogues of eledoisin described in the literature were obtained by substituting amino acids in the peptide chain or by shortening it. Only little is known about the influence of non-peptidic substituents on the activity. Therefore we investigated the hypotensive activity of several acyl derivatives of the C-terminal eledoisin sequences. The C-terminal heptapeptide H-Asp-Ala-Phe-Ileu-Gly-Leu-Met-NH_2 is approximately four times more active than the C-terminal hexapeptide H-Ala-Phe-Ileu-Gly-Leu-Met-NH_2. But this increase in activity does not depend on original aspartic acid residue in position 5. A number of other α-amino acid residues also cause an increase (two- to fourfold). To clarify the question whether an extension of the peptide chain enhances the activity, we synthesized acyl hexapeptides with the formyl-, caprinoyl-, palmitinoyl-, chloroacetyl-, succinoyl-, hydroxyisovaleryl-, *p*-amino benzoyl-, nicotinoyl-, and n-butylcarbamyl group as acyl residues. The importance of the free amino groups is examined with the Lys^5-heptapeptide H-Lys-Ala-Phe-Ileu-Gly-Leu-Met-NH_2.

The possible acetyl derivatives (α-acetyl-, ε-acetyl-, and α.ε-diacetyl-) and the possible desamino derivates (des-α-amino = ε-amino capronyl-, des-ε-amino = norleucyl, and des = α.ε-diamino = capronyl-) were synthesized.

The hypotensive activity of all the described derivatives will be discussed with regard to the influence of the structure on the biological activity.

27. The Measurement of Kinin-Releasing Enzymes in Plasma. J. MARGOLIS (*Children's Medical Research Foundation, Royal Alexandra Hospital for Children, Sydney, Australia*).

The rapid phase in the release of kinin by plasma kallikrein(s) is a specific reaction which utilises a susceptible part (approximately 25%) of kininogen complex (component B) and involves two distinct components of the releasing enzyme system: component A and Hageman factor (HF). These were measured in terms of μg/min of bradykinin-equivalent (BK-eq) produced from a suitable substrate. Removal of inhibitors by various methods resulted in marked slowing of the reaction and apparent loss of specificity but, with the addition of EDTA and corrections for dilution, temperature, and kininogen content, reproducible results were obtained on intact plasma. In this substrate, activated HF is a potent releasing agent. By fractional elution from kaolin, at pH 11·6, stable preparations were obtained, capable of producing more than 80 μg/min BK-eq/mg enzyme protein at 22° in undiluted systems. This is equivalent to 200 units of kallikrein ('Glumorin' F.B.A.) per mg. Activated HF is inactive in 'B-depleted' plasma which is still a satisfactory substrate for glandular kallikreins. Component A is necessary for the formation of soluble kallikrein in plasma or fractions activated by contact. It was assayed in samples treated with glass or kaolin and an excess of activated HF. The results were expressed either as per cent activity relative to a standard or in absolute units (μg/min/ml). Unexpected discrepancies in the latter led to a re-examination of the kinin-releasing mechanisms in plasma.

28. Automated Peptide Synthesis. R. B. MERRIFIELD (*The Rockefeller Institute, New York, N.Y., U.S.A.*).

In an effort to simplify and accelerate the synthesis of peptides, a new approach to the problem was devised. It was called solid-phase peptide synthesis, and was based on the idea that peptides could be assembled in a stepwise manner while attached at one end to an insoluble solid particle. With the peptide securely bound in the solid phase it was possibly to purify each of the intermediates simply and quickly by thorough washing, rather than by recrystallization or other tedious procedures. The method was applied to the synthesis of bradykinin, methionyl-lysyl-bradykinin, and angiotensin. The products were obtained in good