1. E. AMUNDSEN (*Institute of Physiology, University of Oslo, Norway*).
No abstract received.

2. Hypotensive Peptides from Amphibian Skin. ADA ANASTASI (*Farmitalia, Laboratori Ricerche, Milan, Italy*).

A screening of the skin extracts of more than 200 species of amphibia from all over the world has been made while searching for new biologically active peptides.

The structure and the eledoisin-like action of physalaemin, the first highly active peptide isolated from the skin of the South American amphibian *Physalaemus fuscumaculatus*, have been described. The isolation of a hypotensive peptide from the skin of *Rana temporaria* and its identity with plasma bradykinin have also been reported.

Some interesting new peptides have been found recently which possess eledoisin or bradykinin-like activity or show pharmacological actions which cannot be related to eledoisin or bradykinin. They are studied one by one with regard to their biological and chemical properties. A few of them have already been isolated and their structure determined; the purification of the others is in progress.

Two peptides with eledoisin-like activity have been extracted from the skin of the *Phyllomedusae rohdei* and *hypochondrialis;* the electrophoretic and chromatographic behavior of the second peptide gave evidence of a structure different from that of eledoisin and physalaemin.

Bradykinin-like peptides are present in various species of *Ranae* and *Phyllomedusae*. The skin of *P. rohdei* contains at least three peptides structurally related but not identical with plasma bradykinin. Two of them possess remarkable hypotensive action.

A series of small peptides containing tryptophan which have been named tryptokinins, has been found in the skin of *P. rohdei* and *P. hypochondrialis*. Two of the tryptokinins that do not show activity with the usual pharmacological tests have the following structures: Pyr-Pro-Pro-Try-Val·NH_2; Pyr-Pro-Pro-Try-Met·NH_2.

3. Physiological Influence on the Liberation of Human Plasma Kinin at Low Temperatures. DESIRÉE ARMSTRONG, G. L. MILLS and F. SICUTERI (*Dept. of Pharmacology, Middlesex Hospital Medical School, Univ. of London, England; and Centro Cefalée, The Medical Clinic, Univ. of Florence, Italy*).

The reported kininogen depletions which occurred in "untreated" human serum or plasma samples collected during parturition[1-4] have been shown to be accompanied by accumulation of high concentrations of kinin which parallel the ensuing degree of kininogen depletion.[1,5].

We have now shown[6] that this eruptive accumulation of kinin is initiated by lowering the temperature of the plasma and that it is a manifestation of a general property possessed, in greater or lesser degree, by all human plasma.

Measurements of kininogen depletion, and also of kinin production in the presence of kininase inhibitors, show that spontaneous kinin generation is normally minimal at 37°. Its rate then increases as the temperature is reduced below 37°, and can be controlled, at will, by merely lowering or raising the temperature.

We have attributed the mechanism of this "cold accelerated reaction" to changes in the structure of the human kininogenase molecule, or a precursor, which are brought about by the dissociation of hydrophobic bonds. In plasma at 37° these bonds tend to maintain the enzyme in an unreactive state. But, having a positive enthalpy of formation they are weakened by a fall in temperature, which thus leads to changes in the configuration of the enzyme and so to the revelation of the kininogenolytic property.

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4. Immunologic Studies of Components of the Kallikrein–Kinin System. C. W. AUNGST, N. BACK, B. CASTILONE and G. A. TSUKADA (*The Roswell Park Memorial Institute, and the State Univ. of New York, Buffalo, N.Y., U.S.A.*).

Immunologic studies of crude urinary kallikrein (UKK), purified pancreatic kallikrein (PKK), and synthetic bradykinin (BK) were undertaken. Antisera were prepared in the rabbit by intramuscular injection with Freunds' complete adjuvant. By means of Ouchterlony and immunoelectrophoretic techniques, five bands were revealed when UKK was developed with UKK antiserum and two bands when PKK was developed with PKK antiserum. Eight bands were seen when normal serum was developed with UKK antiserum: two bands in the albumin region, two in the α_1, two in the α_2, and a definite band in the 7S γ-globulin region. Adsorption of

the UKK with normal human serum retained only the α_2 and 7S γ-globulin bands. The PKK–anti-PKK bands were in the α_1 and α_2 globulin regions. No cross reaction was observed between PKK and UKK antiserum or UKK and PKK antiserum. A single band was seen with BK antiserum in a 2% agar when the antigen was applied 2 to 24 hr after application of the antibody. No bands were seen when BK was electrophoresed and developed with BK antiserum. However, a definite precipitant band did appear near the albumin region when normal human serum was developed with BK antiserum. Studies with purer UKK, PKK, and bovine and human bradykininogen are in progress.

Indirect immunofluorescent staining techniques were employed to study the localization of these components in a variety of tissues. UKK and PKK antiserum adsorbed with normal human serum localized onto glandular cells and ducts of human salivary and pancreatic tissue. Localization of BK also was noted. The significance of these results will be discussed. (Supported by U.S. Public Health Service Grant HE-08633, National Heart Institute.)

5. The Role of the Fibrinolysin and Kallikrein–Kinin Systems in Allergic and Anaphylactic Phenomena. N. BACK, H. WILKENS, R. STEGER, A. E. MUNSON and I. B. MINK (*The State Univ. of New York at Buffalo, and the Roswell Park Memorial Institute, Buffalo, N.Y., U.S.A.*).

The nature of the biochemical lesions seen in allergic and anaphylactic phenomena has been under investigation. The activation of the fibrinolysin system and the concomitant appearance of circulating kinin activity during the acute stage of anaphylaxis in the dog has been reported (Back *et al., J. Amer. med. Ass.* **183,** 260, 1963). This report details the interrelationships of the fibrinolysin, kallikrein–kinin, and blood coagulation systems in experimental allergic phenomena, and the influence of inhibitors of these systems on the course of the shock state.

Animals (dogs, guinea pigs, mice) were sensitized with appropriate antigens and anaphylaxis induced two weeks later. In the dog such physiologic parameters as venous and arterial blood pressure, respiration, electrocardiogram, and smooth-muscle activity were monitored continuously during the shock state. Simultaneous serial analyses of factors of the kallikrein-kinin, fibrinolysin, and blood coagulation systems were made. Anticoagulation and fibrinolysis involving thrombocytopenia, and decreases in levels of prothrombin, factor V, and fibrinogen were noted. Thrombelastographic studies revealed fibrinolysis with decreases in plasma plasminogen and antiplasmin levels. Histamine and kinin release occurred, as well as an increase in kininase activity. Isolated perfused hind limb preparations from sensitized dogs were established to study the effect of various pharmacologic agents on local and systemic response to anaphylaxis, kinin, kallikrein, plasmin, and anoxia.

The effect of kallikrein-kinin inhibitors, plasmin inhibitors, anticoagulants, and antihistaminic and antiserotonin agents on the course of the anaphylaxis also will be reported. Some of the agents studied included Trasylol, antiplasmin, ϵ-amino caproic acid, soybean and lima bean trypsin inhibitor, ovomucoid, antipyretic analgesics, heparin, and Dicumarol. (Supported by U.S. Public Health Service Grant HE-08633, National Heart Institute.).

6. Effects of Eledoisin and Bradykinin on General and Visceral Circulation. A. BERETTA ANGUISSOLA, F. S. FERUGLIO, S. CAMPUS, L. CHIANDUSSI, G. PANDOLFO and G. BERT (*Istituto di Patologia Speciale Medica e Metodologia Clinica dell' Università di Torino, Turin, Italy*).

Eledoisin (0.01 μg/kg/min) was administered i.v. to mongrel dogs. Cardiac output and general vascular resistance decreased significantly. The substances had negligible effects on the pulmonary circulation. The visceral circulation changed as follows. (a) The cerebral blood flow showed a slight decrease; the O_2 consumption was unaltered. (b) The coronary blood flow increased significantly; the O_2 consumption showed slight increase. (c) The hepatic blood flow showed a conspicuous increase with a marked reduction of vascular resistance. (d) The renal blood flow did not change significantly.

Bradykinin (0·5 μg/kg/min) was administered i.v. to mongrel dogs and to normal human subjects. The arterial pressure showed a constant reduction. The cardiac output decreased slightly in the anesthetized dog, but increased in unanesthetized man. The visceral circulation changed as follows. (a) The cerebral blood flow and resistance in the dog changed little. (b) Some preliminary data suggest an increase in the dog's coronary blood flow. (c) The hepatic blood flow of normal human subjects showed a slight increase which is not statistically significant. (d) In both men and in dogs the renal blood flow increased significantly.

7. Self-Antagonism of Bronchoconstriction Induced by Bradykinin and Angiotensin. H. O. J. COLLIER (*Dept. of Pharmacological Research; Parke Davis & Co., Hounslow, Middlesex, England*).

Bradykinin and angiotensin release catecholamines from the adrenal glands in cat, dog, rabbit, and rat.[1–3] With bronchoconstriction as an indicator, recent experiments have shown that bradykinin and angiotensin also release cate-