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-

cholamines from the adrenal glands of guinea pigs.[4] Release of catecholamines by bradykinin should be taken into account in interpreting the actions of bradykinin on respiration and the features of anaphylactic bronchoconstriction in the guinea-pig. For example, this effect probably explains the incompleteness of the bronchoconstriction induced by bradykinin compared with that induced by 5-hydroxytryptamine.[5,6] Likewise, it may explain the bronchodilatation sometimes induced by bradykinin after suppression of its bronchoconstrictor action by nonsteroidal anti-inflammatory drugs.[7] Again, the release by bradykinin of endogenous catecholamines must introduce uncertainty into interpretation of the effects of administered catecholamines on responses to bradykinin.

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8. Role of Bradykinin and Bradykinin-like Substances in the Genesis of Some Types of Cardiovascular Shock. A. P. Corrado (*Dept. of Pharmacology, Faculty of Medicine of Ribeirão Preto, Univ. of São Paulo, Brazil*).

Beraldo[1,2] was the first to suggest an activation of the enzymatic system *in vivo* which releases bradykinin in peptone or anaphylactic shock in dogs where an increase in blood bradykinin was observed. These results were corroborated by Brocklehurst and Lahiri[3] in guinea pig, rabbit, and rat anaphylaxis. A bradykinin-like substance was also detected in the blood of dogs during cardiovascular shock produced by the injection of proteolytic enzymes from bacteria or mammals.[4,5]

Bradykinin (or a bradykinin-like substance) is rapidly inactivated[6] by plasma and tissue kininases.[7–9] Therefore, the values of the plasma levels of the polypeptides released during cardiovascular shock are preferably determined in terms of the precursor bradykininogen.[4,10–15]

By measuring the kininogen under these conditions we have found a very good relationship between the amount of released polypeptide and the severity of the cardiovascular shock produced in dogs in experimental anaphylaxis, acute pancreatitis, and endotoxin shock.

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9. Possible Modes of Kinin Formation in Some Pathological States in Man. V. Eisen and C. A. Keele (*Dept. of Pharmacology, Middlesex Hospital Medical School, London, England*).

We shall discuss three conditions in which plasma kinin formation appears to be of clinical importance.

1. Transfusions of human plasma fractions containing fibrinogen and factor VIII produce in some patients adverse reactions which resemble the effects of bradykinin.[1] Analyses of such fractions[2,3] have shown that they contain plasminogen, preactive factor XII, and a small amount of kininogen. The observed clinical reactions, however, appear to be due to the presence of active plasma kallikrein; 100 Frey units or more may be introduced with some clinical transfusions. Moreover, the fractions contain an enzyme resembling C'1-esterase, which may also cause reactions.

2. Seegmiller[4] has reported that in gout the phagocytosis of urate microcrystals by the leukocytes in synovial fluid leads to kinin forma-