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-

tion and thus to acute gouty arthritis. Evidence will be presented that urates also induce kinin formation in inflammatory joint fluid by a purely humoral mechanism which—like intrinsic plasma kinin formation—involves factor XII and plasma kallikrein.

3. There is a growing number of diseases in which a pathogenetic role is claimed for released lysosomal enzymes. Such release results from phagocytosis, immunological or bacterial attack, or physicochemical cell injury or death.[5] We have shown that lysosomal enzymes may induce significant kinin formation directly, or indirectly through constituents of digested tissues. Pathological processes may also be influenced by the potent kinin-destroying action of some lysosomal endopeptidases.

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**10. Studies of the Metabolism of Bradykinin.** E. G. ERDÖS and H. T. YANG (*Dept. of Pharmacology, Univ. of Oklahoma School of Medicine, Oklahoma City, Okla., U.S.A.*).

Various aspects of the enzymatic metabolism of bradykinin and its analogues have been investigated. As in other animals, i.v. injection of carboxypeptidase B blocked the effects of bradykinin, kallidin, and met-lys-bradykinin in the rat by rapidly destroying the peptides in the circulation. On the other hand the hypotensive activity of bradykinin in the rat was greatly enhanced by pretreatment with the inhibitor, mercaptoethanol. In the cat repeated injection of purified pancreatic carboxypeptidase B resulted in a long-lasting blockade against the effects of bradykinin on the blood pressure. (The pancreatic carboxypeptidase used was obtained in the form of a dry, stable preparation.) When the injected enzyme disappears from the blood, it is taken up by the kidney and to a certain extent by the liver of various laboratory animals. Injected carboxypeptidase B was also recovered from the urine of rats and guinea pigs.

The normally occurring carboxypeptidase in blood plasma has not only a peptidase but an esterase activity as well.

In addition to blood plasma as a homeostatic mechanism, kidney contains several enzymes capable of inactivating bradykinin. Among them the properties of a prolidase (imidopeptidase) and a carboxypeptidase have been investigated.

The identification and purification of another kidney enzyme is in progress. (This work was supported in part by Grants HE-08764 and NB-05196 from the National Institutes of Health, U.S.P.H.S.)

**11. Active Polypeptides in the Amphibian Skin.** V. ERSPAMER and G. BERTACCINI (*Institute of Pharmacology, University of Parma, Italy*).

Amphibian skin, which is often an enormous storehouse of biogenic amines, may also contain large amounts of highly active polypeptides. The species richest in these compounds belong to the genera *Rana* and *Phyllomedusa*, but strong activities have been found also in some species of the genera *Hyla*, *Leptodactylus*, and *Ascaphus*. Sometimes the biological activity is determined by a single polypeptide, but in other instances it is the result of the combined activities of different constituents. In this case their separation is imperative. In the identification of new polypeptides and their distinction from each other, parallel bioassay on six or seven test objects has been routinely employed, together with enzymic treatments. The main results of our studies were as follows: (a) authentic bradykinin is the active polypeptide of *Rana temporaria* and possibly of other *Rana* species; (b) *Physalaemus fuscumaculatus* and other *Physalaemus* species contain physalaemin, a tremendously potent hypotensive undecapeptide, strictly related to eledoisin; (c) *Ascaphus truei* contains large amounts of a bradykinin-like polypeptide, surely different from authentic bradykinin; (d) finally, *Phyllomedusae* show the most complicated spectrum of polypeptide activities, because their skin contains physalaemin-like polypeptide(s), at least three bradykinin-like polypeptides, and a polypeptide possessing an unusually long-lasting hypotensive action.

Various data on the amino acid composition and sequence of these polypeptides have been collected, and the synthesis of some of them is in progress.

**12.** JULES A. GLADNER (*National Institutes of Health, Bethesda, Md., U.S.A.*).
No abstract received.

**13. Cardiovascular Actions of Physalaemin.** A. GLÄSSER (*Farmitalia, Laboratori Ricerche, Milan, Italy*).

The cardiovascular actions of physalaemin, a new undecapeptide chemically related to eledoisin, were investigated on dogs and on other animal species. Comparison with eledoisin and other vasodilator agents was made in dogs while the systemic blood pressure and coronary and hind limb blood flows were recorded.