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.

1. W. d'A. MAYCOCK *et al.*, *Brit. J. Haemat.* **9**, 215 (1963).
2. M. MACKAY, W. D'A MAYCOCK, E. SILK and B. S. COMBRIDGE, *Brit. J. Haemat.* In press (1965).
3. V. EISEN, *ibid.*
4. J. E. SEEGMILLER, Lecture at The Royal Society of Medicine, London (1964).
5. A. V. S. DE REUCK and M. P. CAMERON, *Lysosomes*. Churchill, London (1963).

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.

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.

1. L. G. GOODWIN and W. A. G. RICHARDS, *Brit. J. Pharmacol.* **15**, 152 (1960).
2. W. H. G. RICHARDS, *Brit. J. Pharmacol.* **24**, 124 (1965).

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