yields and were shown to be chemically pure and biologically active. Solid-phase peptide synthesis has now been automated in collaboration with Dr. John Stewart. All the reactions were carried out in a single reaction vessel and each of the manipulations was performed in the proper sequence under the control of a pre-set programmer. A peptide chain can be lengthened by six amino acid residues per day completely automatically without manual attention. The process was tested on the synthesis of bradykinin and gave satisfactory results.

29. Human Salivary Kallikrein and Liberation of Colostrokinin. HIROSHI MORIYA (*Laboratory of Physiological Chemistry, Tokyo College of Science, Shinjuku-ku, Tokyo, Japan*).

The isolation and purification of kallikrein from human pooled saliva (Japanese) has been studied. The kallikrein content in saliva was 1–2 Frey U/ml. Acetone-dried powder of human mixed saliva was found to be suitable as starting material for purification. A highly purified fraction was obtained by using ion-exchange column chromatography, acetone fractionation, and Sephadex filtration. The activity of kallikrein was assayed by measuring the esterase activity with TAME substrate and the increase in arterial blood flow of dogs. The purest preparation obtained had 200 Frey U/mg with a yield of 0·2–0·5 FU/ml of original saliva. Human salivary kallikrein liberates colostrokinin from bovine colostrum as measured on the rat uterus and dog blood pressure. Human salivary kallikrein was labeled with ^{131}I; its effect on absorption through the intestinal wall was also studied.

30. Bradykinin in the Carcinoid Syndrome. JOHN A. OATES, WILLIAM A. PETTINGER and R. B. DOCTOR (*Division of Clinical Pharmacology, Depts. of Medicine and Pharmacology, Vanderbilt Univ. School of Medicine, Nashville, Tenn., U.S.A.*).

Previously we have demonstrated that a kinin peptide is released into the circulation of some patients with carcinoid syndrome after the injection of epinephrine. The present investigations were carried out to characterize this peptide. By gradient elution chromatography on CM-Sephadex, it was possible completely to separate microgram amounts of bradykinin from kallidin. The elution characteristics of the carcinoid kinin in this system were identical with those of authentic bradykinin. On both high-voltage electrophoresis at pH 3·5 and paper chromatography with butanol: acetic acid:H_2O, the carcinoid kinin had the same mobility as bradykinin. The rate of inactivation during incubation with chymotrypsin for 12 min at 12° was the same for both the carcinoid kinin (22·7%) and bradykinin (22%). Very little inactivation of either occurred during incubation with trypsin for 60 min at 38°. The pharmacologic effects of the carcinoid kinin and bradykinin on the rat uterus, guinea pig ileum, rabbit blood pressure, and rat duodenum were also similar. All these studies indicate that the kinin found in the hepatic vein blood of patients with carcinoid syndrome is bradykinin. There is additional evidence suggesting that the tumor kallikrein initially forms kallidin which is rapidly converted to bradykinin in plasma.

31. Observations in vivo of the Peripheral Circulation During Bradykinin Infusion by Transilluminating Quartz-Rod Technique (colored motion picture). G. PELLEGRINI and C. PIOVELLA (*Instituto di Patologia Medica dell'Università di Pavia, Italy*).

The terminal circulation of the mesentery and liver of rats and frogs was studied during and after bradykinin infusion. After an initial vasoconstriction, a large dilatation of the small arteries was observed, together with a spastic vasoconstriction. The irregular shape of the capillaries with an increase in permeability was demonstrated by fluoroscopy.

32. Bradykininogen in the Blood of Women During Pregnancy, Labor, and Puerperium. P. PERITI and F. GASPARRI (*Instituto di Farmacologia, and Instituto di Clinica Ostetrica e Ginecologia, Università di Firenze, Italy*).

Bradykininogen (BKG) of the plasma has been assayed with a biological method using rat uterus *in vitro*. During pregnancy BKG increases and at the ninth month reaches above normal levels with an arteriovenous ratio significantly greater than unity.

At the onset of labor BKG decreases progressively as the uterine contractions become more intense. The decrease reaches its maximum in the expelling stage. Within a few hours of the delivery, BKG values return to normal.

Twelve to twenty-four hours after the delivery the level of BKG starts a slow, progressive decrease which lasts three to four days, reaching in some cases below normal values. Within eight to ten days after the delivery BKG returns to normal in women who have had no puerperal complication.

The fetus is born with a BKG content of the blood markedly lower than the normal average value in the adult. During the first week of life, BKG slowly rises toward a higher level.

The hypothesis is suggested that the behavior of BKG in the woman during pregnancy and labor is connected with the uterine muscular mass and with its prolonged rhythmic contraction in the dilating and expelling stage of labor. In puerperium

the cause seems to be the uterine involution and the trauma of the delivery.

The low BKG content of the fetal blood at birth and in the first days of extrauterine life could reflect the immaturity of the liver in the newborn.

33. The Purification and Some Properties of Human Plasma Kallidinogen. JACK V. PIERCE and MARION E. WEBSTER (*Laboratory of Metabolism, and Laboratory of Cardiovascular Physiology, National Heart Institute, Bethesda, Md., U.S.A.*).

Kallidinogen, a plasma α_2-globulin which produces kallidin or bradykinin when treated with kallikrein, trypsin, or snake venom, has been purified about 400-fold over the starting human plasma and in 10% yield. This was accomplished by the following four steps: (1) DEAE-cellulose chromatography and (2) rechromatography, (3) hydroxylapatite chromatography, and (4) Sephadex G-200 gel filtration. Linear gradients of phosphate buffer were used in steps (2) and (3). Step (2) gave two peaks of activity in a ratio of 3·9. Step (3) on the combined activity from (2) also gave two peaks, I and II in the order of their elution, but in a ratio of 0·7. Gel filtration of peak I gave a major activity peak with a K_d of 0·46 and a minor peak with a K_d of about 0·23. Peak II on the same G-200 column gave only one activity peak (K_d = 0·45), from which the purest material was obtained. Hydroxylapatite chromatography of peak II material, with a linear gradient of phosphate buffer in the presence of 1 M sodium chloride, also gave two peaks of activity in a ratio of about 1·0. Experiments are being done to clarify this confusing situation. Studies of the physicochemical and biochemical properties of kallidinogen will be made as soon as material satisfying several criteria of homogeneity has been obtained.

34. Characterization of Kinins in Wasp Venom. J. L. PRADO,* Z. TAMURA,† E. FURANO, J. J. PISANO and S. UDENFRIEND (*Laboratory of Clinical Biochemistry, National Heart Institute, Bethesda, Md., U.S.A.*).

At least six kinin fractions were observed when wasp venom preparations (genus *Polistes*) were chromatographed on columns of carboxymethyl cellulose and carboxymethyl Sephadex. The first two kinins had pharmacological and chemical properties similar to bradykinin and kallidin respectively. However, when the fluorescent dimethylnaphthylsulfonyl (dansyl) derivatives were examined by thin-layer chromatography (TLC) several biologically active fluorescent bands were observed, none of which corresponded exactly to dansyl bradykinin or dansyl kallidin. The fluorescent peptide derivatives had 1–2% the potency of the free peptide in the estrous rat uterus assay. Most of the kinin activity of venom (>50%) was in fraction 3 which consisted of a single peptide as revealed by TLC of the dansyl derivative. It had the amino acid composition: Arg_2, Asp, Gly_2, Glu, Leu, Lys_2, Phe_2 Pro_3, Ser, Thr. Chymotrypsin but not trypsin destroyed biological activity. An active peptide was isolated from the tryptic digest. It was composed of Arg_2, Gly_2, Phe_2, Pro_3, Ser, with glycine the N-terminal amino acid. The peptide was indistinguishable in chemical and biological tests from synthetic glycylbradykinin, also termed gly^1-kallidin (Schröder and Hempel, *Experientia, Basel* **20**, 529, 1964). To be determined are the amino acid sequence of undigested fraction 3 and the structures of the kinins in the other fractions. (Reference peptides were kindly supplied by E. Nicolaides and E. Schröder.)

* Fulbright-Hays visiting scholar on leave of absence from Escola Paulista de Medicina and Instituto Adolfo Lutz, São Paulo, Brazil.
† Visiting scholar from the faculty of Pharmaceutical Sciences, University of Tokyo, Japan.

35. Kallikrein in the Submaxillary Gland. M. SCHACHTER (*Dept. of Physiology, Univ. of Alberta, Edmonton, Alberta, Canada*).

Shortly after salivary kallikrein was described (Werle and Roden, 1936), it was suggested that this substance was the mediator of chorda-tympani-evoked vasodilatation in the submaxillary gland and tongue (Ungar and Parrot, 1936). This suggestion was made to explain the fact that vasodilatation in the gland caused by stimulation of the chorda-tympani nerve is not blocked by doses of atropine, which readily block the secretory response. Further work led to the specific conclusion that vasodilatation in the active gland is secondary to secretion; i.e. it is caused by kallikrein passing from the secretory cells into the tissue spaces where it releases the vasodilator peptide, kallidin (Hilton and Lewis, 1955, 1956, 1958).

Our experimental results listed below, however, have led us to conclude that vasodilatation produced in the submaxillary gland by stimulation of the chorda-lingual nerve is *not* mediated by kallikrein, but that true vasodilator nerve fibres, probably cholinergic, are present in this nerve.

In the cat. (a) The vasodilatation resulting from close arterial injection of dialysed cat saliva into the salivary gland with intact blood circulation differs from that caused by stimulation of the chorda-lingual nerve or by acetylcholine (ACh) similarly injected: it is slower in onset, it is not so great, and it is generally more prolonged. (b) Desensitization of the blood vessels to the vasodilator action of a standard dose of bradykinin