pronounced in SCS cells with prominent diastolic depolarization. These observations could be accounted for by a specific increase in K^+ conductance in cells in which the K^+ equilibrium potential is less than maximal diastolic potential. (Supported by U.S. Public Health Service Grants HE 08372-02, HE 05435-05, and MH 3477.)

46. Synthesis of New Isomers of Bradykinin. K. VOGLER (*Hoffmann-LaRoche, Inc., Basle, Switzerland*).

In this study the synthesis of new isomers of the natural hormone containing D-amino acids is reported. Both all-D-bradykinin and all-D-retro-bradykinin were obtained in a pure state. The former represents the first synthetic antipode of a polypeptide hormone. The biological properties of these new compounds are discussed in the light of stereochemical considerations.

47. Demonstration of the Presence in Human Plasma of Two Separate Kinin-Forming Systems. W. VOGT (*Medizinische Forschungsanstalt der Max Planck Gesellschaft, Göttingen, Germany*).

It is well established that human plasma contains plasma kallikrein which, by acting on "kininogen", liberates plasma kinin. In addition another kinin-forming enzyme is present for which the term "kininogenase II" is suggested. It acts specifically on a substrate different from that utilized by kallikrein. This substrate (kininogen II) is not attacked by plasma kallikrein (suggested name "kininogenase I") or by pancreas kallikrein or trypsin. Kininogenase II is present in plasma as an inactive precursor and is activated by trypsin or by contact with glass. Active kininogenase II activates kininogenase I and hastens the subsequent destruction of the latter in plasma.

It seems likely that kinonogenase I is not activated by glass contact (or by Hageman factor) directly, but only through activation of kininogenase II. This would explain why dog plasma cannot be induced to form kinins on contact with glass. Dog plasma contains kininogenase I but practically no kininogenase II. In contrast, rat plasma contains only the kinin-forming system II. It is therefore a poor substrate for trypsin but well activated by contact with glass.

After glass activation of human plasma (B-depletion) kininogenase II and kininogen I are left, kininogenase I being inactivated and kininogen II being used up. For this reason in such plasma no kinin can be formed on further incubation, although by different methods an enzyme as well as a substrate can be demonstrated.

48. Polypeptide Receptor Mechanisms; Influence of pH and Heat. EDWARD J. WALASZEK and DONALD C. DYER (*Dept. of Pharmacology, Kansas Univ. Medical Center, Kansas City, Kans., U.S.A.*).

The biological testing of polypeptides was carried out on the isolated guinea pig ileum in a modified Tyrode's solution at 35°. The effect of pH was studied on the contractile potency of four polypeptides: bradykinin, eledoisin, angiotensin, and substance P. The solution used was Tyrode's without $NaHCO_3$, the pH of the solution adjusted with 0·1 N HCl or 0·1 N NaOH. The pH values were varied from 5 to 10. When bradykinin, eledoisin, and angiotensin were tested together, a clear dichotomy could be seen: at low pH eledoisin was least potent, whereas bradykinin was the most potent, peptide. As the pH was increased eledoisin increased in potency very markedly, while bradykinin declined in potency. Angiotensin tended to remain reasonably constant. It was sometimes found that at pH 10 bradykinin had no effect, whereas eledoisin was still very active. We suggest that it is possible to differentiate eledoisin from bradykinin by this procedure. It would appear that the positive charge is more important for bradykinin activity than it is for eledoisin activity. This could then be interpreted that they are acting on two different receptors. Substance P resembled eledoisin in these studies.

In another phase of this study the effect of heat on actions of different polypeptides on the guinea pig ileum were observed. These results will be reported in detail.

49. The Physiological and Pathological Role of the Kallikrein–Kallidin System. MARION E. WEBSTER (*Laboratory of Cardiovascular Physiology, National Heart Institute, Bethesda, Md., U.S.A.*).

The biochemical characterization of the kallikrein–kallidin system has led to speculation that the endogenous release of these powerful vasodilator polypeptides may play a role in regulating local blood flow. Infusion of the polypeptides directly into the kidney, coronary circulation, skeletal muscle, etc., is associated with an increase in blood flow independent of any systemic effects. The demonstration, however, that infusion of a naturally occurring substance can influence local blood flow, does not necessarily indicate that it alters blood flow under physiological conditions. Thus, for example, the vasodilatation produced in skeletal muscle by muscle contraction, arterial occlusion, and lumbar cholinergic sympathetic nerve stimulation is not altered in the presence of carboxypeptidase B, although that produced by infused kallidin is effectively blocked. The kallidins, therefore, do not appear to contribute to the vasodilatation seen under these conditions.