A detailed report on the isolation and characterization of polycyclic aromatic substances from barnacles will be given elsewhere.

References

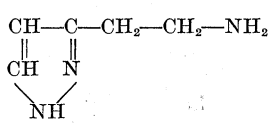
1. SHIMKIN, M. B., and BRYAN, W. R. *J. Natl. Cancer Inst.*, **4**, 25 (1943).
2. SHIMKIN, M. B., and ANDERVONT, H. B. *J. Natl. Cancer Inst.*, **1**, 57 (1940).
3. BRYAN, W. R., and SHIMKIN, M. B. *J. Natl. Cancer Inst.*, **3**, 503 (1943).

An Analog of Histamine that Stimulates Gastric Acid Secretion without other Actions of Histamine

C. E. Rosiere and M. I. Grossman

Department of Clinical Science,
University of Illinois, College of Medicine, Chicago

During a survey of the stimulatory and inhibitory actions of chemical analogs of histamine on gastric secretion, one compound was found that possessed the unique property of stimulating gastric acid secretion without producing any of the other pharmacologic actions of histamine. The compound is 3-(β ethylamine) pyrazole (compound XXIV). Its structural formula is:



It will be seen that this is an isomer of histamine in which the ring has a pyrazole instead of an imidazole configuration. The relationship of the side chain to the =N— is the same as in histamine. The compound was first synthesized and studied by Lee and Jones (*1*), who found that it did not contract the isolated guinea pig ileum and that it did not lower blood pressure in cats. In the anesthetized dog we have found compound XXIV to be about 1/700th as potent as histamine in depressing blood pressure.

Compound XXIV stimulates acid secretion in dogs with pouches of the entire stomach when the hydrochloride is administered subcutaneously, intramuscularly, intravenously, or orally. By the subcutaneous route the ED_{50} of the hydrochloride (dose required to produce 50% of the maximal secretory rate) is 8 mg/10 min in comparison with 0.12 mg/10 min for histamine diphosphate. The maximal secretory rate attainable with compound XXIV is the same as with histamine. The pepsin concentration of the juice secreted in response to compound XXIV is not significantly different from that stimulated by histamine.

The hydrochloride of compound XXIV has been injected into 20 human subjects by the subcutaneous and intramuscular routes in doses of 10–50 mg. In no instance have any of the characteristic side effects of histamine been observed, including triple response at site of injection, headache, or flush. The 50-mg dose produced a greater output of HCl than 0.01 mg/kg of histamine diphosphate. Doses of 100 mg produce side effects similar to those seen with histamine.

The existence of this histamine analog with specificity for site of action is in keeping with the known differences between the action of histamine on the gastric glands and its action at other sites. These include (*a*) failure of antihistaminic drugs to counteract action of histamine on gastric glands, and (*b*) inhibition by xanthine alkaloids of actions of histamine at other sites but potentiation of the gastric secretory action.

Compound XXIV may prove useful for routine clinical testing for achlorhydria, not only because it would eliminate the undesirable side reactions that follow histamine, but also because it would be possible to produce stronger stimulation of acid secretion and thus provide more clear-cut results in borderline cases. It may also prove useful for the investigation of the maximal secretory capacity of the human stomach in health and disease.

Reference

1. LEE, H. L., and JONES, R. G. *J. Pharmacol. Exptl. Therap.*, **95**, 71 (1949).

Recovery of Tumor Cells from Effects of the Tumor-inducing Principle in Crown Gall

Armin C. Braun

Laboratories of the Rockefeller Institute for Medical Research, New York

When the tumor-inducing principle associated with the crown-gall bacterium acts on cells of plant species such as *Helianthus annuus* (*1*) and *Vinca rosea* (*2, 3*), an abrupt and irreversible change in the behavior of these cells occurs. Following the transformation process, proliferation of the altered host cells becomes an automatic process that is independent of the inciting bacteria. The cells of the resulting neoplasm are characterized by excessive powers of proliferation and limited powers of differentiation. Competence for organization appears to have been lost as a result of the action of the tumor-inducing principle. Tumor cells of this type are transplantable, and when bacteria-free fragments are implanted into a healthy host they develop into typical uncoordinated crown-gall tumors.

When, on the other hand, this same tumorogenic principle acts on cells located close to the top of a plant species such as *Kalanchoe daigremontiana,* the altered cells appear at first to be of an undifferentiated type. As the tumors grow, however, there results, in place of the characteristic neoplasm, an overgrowth composed not only of uncoordinated tumor cells but of cells that are organized into morphologically complex structures (*4*). The question as to whether these structures result from the growth of normal cells that have been stimulated to develop by the expanding tumor, or whether the morphologically abnormal shoots are composed of altered cells that have acquired a ca-