Figure 1 is a photomicrograph of the tip of a multiple-bore electrode that is currently in use in these laboratories. It was made by packing seven pieces of 3-mm o.d. tubing inside a 9.6-mm i.d. tube. A diametrically opposite pair of bores is used to form salt bridges to silver-silver chloride electrodes inserted into the large ends of the bores. It is also possible to fill two or more of the bores with indium-tin alloy following the technique of Dowben and Rose (*2*).

VINCENT A. VIS

*Department of Physiology,*
*University of Michigan, Ann Arbor*

**References**

1. L. Elson, *J. of Sci. Inst.* **30**, 140 (1953).
2. R. M. Dowben and J. E. Rose, *Science* **118**, 22 (1953).

24 May 1954.

## Anxiety Reduction as a Measure of the Analgesic Effectiveness of Drugs

A method that shows considerable promise for testing the analgesic potency of drugs has been developed recently at this laboratory. Previous techniques involving animals have been dependent upon measuring drug-produced changes in reflexes or unconditioned responses. In contrast with these techniques, the present method provides a testing situation more analogous to that found in the clinic, because it is based upon a psychological principle that has been validated on man.

Previous studies of this series were designed to test the hypothesis that one necessary action of a potent analgesic is the reduction of anxiety associated with anticipation of pain [H. E. Hill *et al., Arch. Neurol. Psychiat.* **67**, 612 (1952)]. These investigations on man demonstrated that therapeutic doses of morphine (15 mg) significantly reduce behavior-disrupting anticipatory responses to painful stimuli. However, these techniques are not practical for the routine testing of drugs, since they are severely penalizing and utilize relatively large numbers of human subjects. It appeared possible, however, to develop a similar method for use with the laboratory rat.

Albino rats, maintained at approximately 70 percent of satiation weight, were conditioned to press a bar at a rapid rate in a modified Skinner Box. Food pellet reinforcements were available aperiodically at approximately 2-min intervals. Bar-pressings were recorded cumulatively on a slowly moving kymograph for the 20-min period of each test. After approximately 15 daily sessions, when the animals showed a high degree of conditioning, a 60-cy/sec tone was introduced 10 min after each test was begun. The tone was of 4 min duration and was terminated by a strong electric shock delivered to the rat through the grid floor. This superimposed, classical conditioning procedure reduced bar-pressing during the tone to a mean of 11 percent of the pretone rates. Subcutaneous injections of morphine, 4 to 11 mg/kg, spaced at weekly intervals restored the inhibited bar-pressing to 22 to 80 percent of the response rate exhibited prior to the tone. The effect varied directly with the dose, despite some over-all decrease in frequency of response.

In general, then, after the animals were thoroughly conditioned, bar-pressing was disrupted or completely inhibited for the duration of the tone. This anticipatory effect of painful stimuli was reduced by morphine with the result that the animals continued to press the bar during the tone. The results are analogous to those of the earlier studies on human subjects and support the hypothesis that reduction of anxiety associated with anticipation of pain is one necessary action of a potent analgesic.

The usefulness of this technique for testing the analgesic properties of a wide range of drugs is currently under investigation. In contrast with other techniques in which animals are used, this method would appear to be more closely related to those employed in the clinic, since anxiety is an important component of clinical pain. Furthermore, several uncontrolled variables that are present in clinical investigations, such as suggestion and personal interaction, would be eliminated. In addition, the method might be used by pharmaceutical houses and in other settings in which clinical studies are not possible.

HARRIS E. HILL
RICHARD E. BELLEVILLE
ABRAHAM WIKLER

*NIMH Addiction Research Center*
*U.S. Public Health Service Hospital*
*Lexington, Kentucky*

18 January 1954.

*Whenever you look at a piece of work and you think the fellow was crazy, then you want to pay some attention to that. One of you is likely to be, and you had better find out which one it is. It makes an awful lot of difference.*—CHARLES F. KETTERING.