

However, it should be emphasized that the number of journals *frequently* consulted by an individual scientist is not likely to exceed 2 or 3 dozen. Most of the code letters for these journals would soon be memorized, so that it would seldom be necessary to consult a comprehensive list. Then, too, the use of code letters might in time be greatly facilitated if the official code for each journal were included on its pages and covers and if short tables of journal codes for each particular field were made available.

The new-style citations would be especially suitable for use with automatic sorting devices for punched cards and microcards. Microcard libraries might ultimately be mechanized so that "dialing" the citation symbols on a modified telephone dial would cause the desired page or pages to be projected on a screen.

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A Technique for Making Multiple-Bore Microelectrodes

In electrophysiological work, it is often convenient to use two or more electrodes separated by a known, small distance. This communication describes a method of making what is in effect a glass pipette with multiple bores. With the several bores filled with a metallic or electrolytic conductor, the pipette becomes a relatively rugged electrode assembly. The number of bores in the pipette can be at least as many as seven, and the spacing between bores at the tip of the pipette can be made as small as $10\ \mu$ and probably less.

The method is that of Elson (1), who used it to produce multiple-bore capillary tubes. A number of Pyrex tubes about 20 cm in length are packed snugly inside a larger Pyrex tube of similar length. This bundle is then treated as a single tube; any technique that will produce a single-bore microelectrode will, with slight modification, yield a multiple-bore microelectrode. During the drawing, the individual bores (and interstices between tubes) remain open, although the relative proportion of walls and bores is somewhat altered.

The drawing technique used in this laboratory is perhaps worth brief description since it requires only simple apparatus and very little manipulative skill. The drawing is done in three steps, the glass being cooled between drawings. In the first step, the original bundle is heated by an oxygen and gas flame and drawn down to about 1 mm in diameter. The piece is then divided near the center of the reduced portion, and a small, solid knob is formed at the tip of each resulting piece; the knob is to facilitate attachment of the weights that are used in the last two stages of drawing.

For the second drawing, the tapered bundle from the first step is supported in a vertical position with the small part pointing downward. A coil of No. 24

Nichrome wire of inside diameter 3 mm and length 5 mm is slipped over the tip and raised until it surrounds the portion of the tapered, multiple-bore tube, which is 2 mm in diameter. A weight of about 25 g is attached to the tip of the piece by an alligator clip. The nichrome coil is heated by current supplied through a variac and a step-down transformer. The coil temperature is regulated so that the glass is slowly drawn out. When an elongation of about 6 mm has been produced, the current is turned off; the glass is not allowed to break. It is advisable to place a small shelf beneath the weight to stop the drawing when the desired elongation has been accomplished. The coil is then lowered 2 or 3 mm until it is centered on the necked-down portion of the glass.

For the third stage of drawing, a heavier weight is attached, the size of which determines the final tip diameter. The coil is heated to a dull red and the glass is allowed to break, after which the current is turned off. The piece that breaks off can be conveniently examined under the microscope.

Since the final tip diameter depends upon several variables, no precise statement can be made regarding the amount of weight to be used in the third stage. The usable range is about 50 to 900 g, corresponding very approximately to 10 and $150\ \mu$, respectively. For a given set of conditions, the tip diameter is reproducible to about 10 percent.

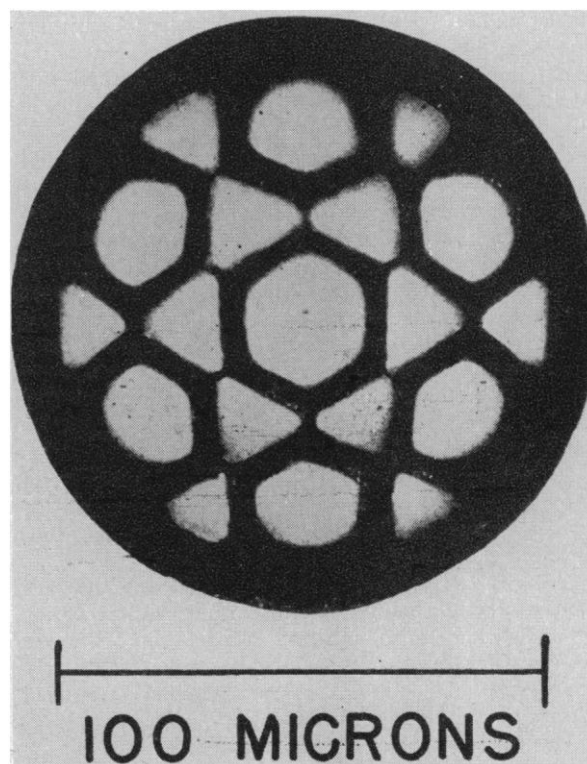


Fig. 1. Photomicrograph of the tip of a multiple-bore glass pipette having one central bore and six others arranged symmetrically around it.

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).

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References

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

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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.

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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.