of acetate (4 mEq/kg/hr), the TmPAH rose from 6.4 mg/min to 12.3 mg/min. In another animal, the control Tm was 5.8 mg/min. It dropped to 1.8 mg/min after phenylbutazone was given and rose to 5.9 mg/min after the administration of Na acetate (8.9 mEq/kg/hr). (See Table I, Exp. B). Thus, it would seem that the rapid intravenous infusion of Na acetate will partially or wholly reverse phenylbutazone inhibition of TmPAH as measured by clearance studies. It has previously been shown to reverse Caronamide inhibition.

In the first experiment, intravenous phenylbutazone (200 mg/kg) caused marked hyperventilation, hemolysis, coma and terminal bloody diarrhea. A subsequent reduction in dose to 50 mg/kg in the priming solution and 50 mg/kg/hr in the sustaining solution was well tolerated in 2 experiments. In 2 other dogs, this dose caused hyperventilation followed by coma. Autopsy of 2 dogs was unrevealing as to the cause of death. The remaining animals were sacrificed immediately after the experiment.

Summary. Phenylbutazone blocks PAH transport but does not affect thiosulfate excretion. The inhibition of TmPAH by phenylbutazone is reversible by the simultaneous infusion of isotonic Na acetate.

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Mosaic Photography in the Demonstration of Human Synapses (*Boutons terminaux*).* (20507)

WILLIAM C. GIBSON AND V. A. PURKIS. (Introduced by D. H. Copp.)

From Crease Clinic Research Unit and Department of Neurological Research, University of British Columbia, Vancouver, B. C., Canada.

The objective demonstration of human cerebral synapses has long been thought to be of considerable interest and importance. However, at the high magnifications required (approximately 2000 x) it has been difficult, in one photomicrograph, to show a convincing number of synapses. As a result, drawings have usually been resorted to, and photographic proofs of the size and distribution of the *Boutons terminaux* have been wanting.

The branching nature of nerve cells has also served to make difficult the picturing, in any single photograph, of the synapses on the dendrites. In many instances the number and location of synapses on the dendrites may be more important that on the "cell body," narrowly interpreted.

The thickness of frozen section of nervous tissue for silver staining (approximately 15 μ) allows one to follow the dendrites great distances, at times. Thinner sections are not very practical since metallic stains make them brittle and since nerve cell processes

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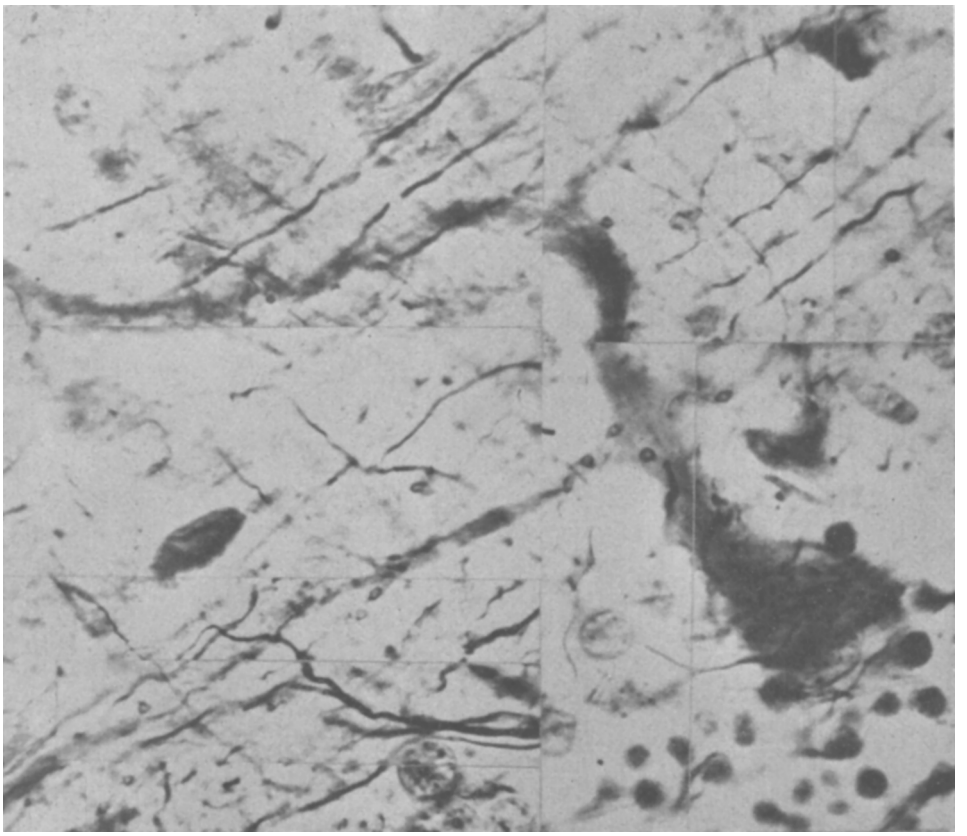

FIG. 1. Synapses on Purkinje cell, normal human cerebellum. ×2000.

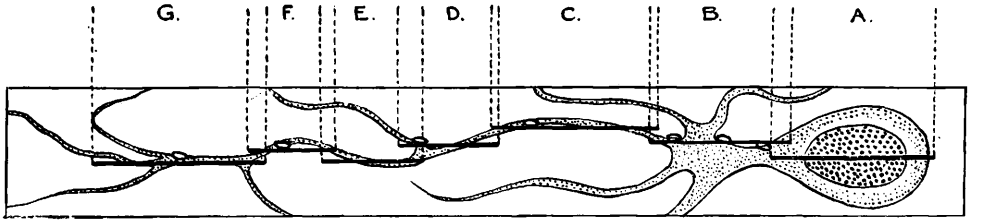

FIG. 2. Cross-sectional sketch of hypothetical cell to show levels of focus required to make up a complete photo-mosaic. Section A of mosaic is taken at level indicated to gain maximal cell diameter, in order that branching dendrites in Section B may be joined in proper perspective. Section E illustrates the fact that in order to preserve continuity of dendrite, photographs must occasionally be taken where synapses are not completely visible.

are sacrificed. For these reasons it was felt that overlap aerial photographic technics might be applied to the synaptic problem. In simplest form, the method is as follows: Each terminal bouton is photographed in focus, a considerable overlap being allowed on either side of it. Occasionally more than one axon terminal can be included in the one focal plane, but for the best results it is usually necessary to treat each bouton ending separately. If a good margin of overlap has been allowed, and if certain desirable landmarks have been consistently included, (capillaries, large thick fibres or cell borders) it is not difficult to assemble the essential parts of each print into a mosaic. In the illustration given here (Fig. 1) 9 separate negatives were used to record the *Boutons terminaux* found at 9 focal planes of a Purkinje cell of a normal human cerebellum stained by Rio-Hortega

double impregnation silver method(1). In this mosaic it has been possible to demonstrate 16 boutons, while a single film would have shown 4 at most. All the processes of the Purkinje cells existing in the 15 μ section could have been followed out by this method if it had been required.

Summary. One solution to the problem of the photomicrographic demonstration of *Boutons terminaux* in the normal human brain is proposed in the form of in-focus mosaic photography.

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The Tetracaine Flare: Differences in Actions of Procaine and Tetracaine on Peripheral Nerve.*† (20508)

R. R. SONNENSCHEIN.

From the Department of Physiology, University of California School of Medicine, Los Angeles.

It is well known that trauma of the skin or the intradermal injection of histamine results in the development of a flare, an area of erythema extending from the site of injection for several centimeters. The studies of Lewis(1,2) and others have established that the flare is brought about by a local nervous mechanism, the so-called axon reflex. In support of this concept is the observation which we have repeatedly confirmed(3,4) that previous infiltration of the skin with the local anesthetic procaine, in the area where histamine is to be injected, prevents the development of the flare, although the local wheal produced by histamine is not affected.

Our attention was drawn(5) to the paradoxical observation that tetracaine, a potent local anesthetic related chemically to procaine, itself produces a flare when injected intradermally even while causing gross anesthesia. This phenomenon appeared to offer the opportunity for testing the concept of the axon reflex as the basis of the flare and for further elucidating its mechanism. The present communication deals with this problem and offers the results of our attempts at its solution.

Material and methods. In all cases, injections of the various agents were made intradermally with 26 or 27-gauge needles in measured volumes from tuberculin syringes. Sterile crystals of procaine hydrochloride‡ and tetracaine hydrochloride‡ were dissolved in sterile isotonic saline to the desired concentrations, expressed as weight/volume. When either agent was injected alone, the volume was 0.1 ml. When the blocking action of procaine on the flare of tetracaine was tested, the former was first infiltrated into the skin in a volume of 0.2 ml, and a few seconds later 0.05 ml of tetracaine solution was injected into the center of the anesthetized area. In all experiments a control was obtained for the dilution factor by injecting the same volume of tetracaine into 0.2 ml of isotonic saline.

To determine the effects of procaine and tetracaine on pain thresholds, the drugs were injected in volumes of 0.1 ml into the skin of the volar surface of the wrist. The thresholds for "fast" (immediate) and "slow" (delayed) pain were determined by use of the warm-wire algesimeter of Lee, Williams and Pfeiffer(6). A bent resistance wire, heated by a battery to various temperatures indirectly indicated by an ammeter, was lightly and briefly applied to the skin. At sub-threshold temperatures only touch was felt. When the threshold for slow pain was reached, the pain was felt after an interval of about one second following the touch. Further increase in temperature finally resulted in elicitation of fast pain occurring simultaneously with the

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