

considerably less denaturation than phenol or tricresol, in the concentrations ordinarily employed for vaccines. It is of practical significance that summer temperatures will shift the equilibrium between native and denatured fractions in favor of the latter, this shift appears to be reversible and the concentration of native protein increases when the temperature is lowered.

8612 P

Pure Monophasic Action Potentials and Their Employment in Studies of Ventricular Surface Negativity.

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Recent interpretations of monophasic action potentials led from an injured and uninjured spot on the ventricular surface hold (1) that the entire deflection is dominated by electrical potential alterations at the *uninjured* spot,¹ (2) that it is essentially influenced by potential variations at the *injured* spot,² or even more specifically, (3) that the initial rise may be governed by electrical variations at the injured region, whereas its rapid offset is determined by the discontinuance of negativity at the normal region.³ Further experimentation makes it apparent that correct interpretations have been hampered by registration of impure monophasic waves, *i. e.*, curves that exhibit oscillations or notches either before the rise or somewhere on the ascending limb, or which give evidence of auricular and other extraneous activity. Previous investigators have been obliged to apologize for inescapable extrinsic effects and to devise explanations to account for them. By recording from a discrete spot of injury, as produced by a new type of suction Ag-AgCl₂ electrode devised by the author, and another Ag-AgCl₂ wick electrode in apposition with the epicardial surface, it proved possible to record consistently monophasic curves that rise acutely from a straight base line and which exhibit no vibrations on the upstroke. An example is displayed in Fig. 1.

¹ Joehim, K., Katz, L. N., and Mayne, Walter, *Am. J. Physiol.*, 1934, **111**, 177.

² Wilson, F., Macleod and Johnston, *Proc. Soc. Exp. Biol. and Med.*, 1933, **30**, 797.

³ Wiggers, H. C., and Wiggers, C. J., *Am. J. Physiol.*, 1935, **113**, 683.

The first purpose of this preliminary communication is to present some evidence that such perfect curves are not influenced by potential changes of the injured area, whereas the so-called extrinsic effects, which appear in the form of notches on the ascending limbs of impure curves are mainly caused by such alterations.

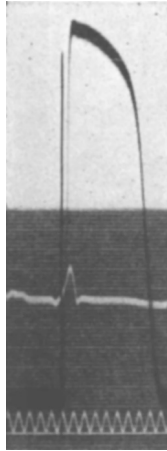


FIG. 1.

Pure monophasic curve from ventricle (large curve) and E.C.G. (lead II). Time, .02 sec.

If monophasic curves from an injured-uninjured region are recorded on paper travelling 100-150 mm./sec. in relation to the waves of a Lead II standard E.C.G., and immediately thereafter monophasic records are taken from the same injured spot and a leg, after the manner of Wilson *et al.*,* then the incidence of the rise of 2 such curves should coincide in all cases regardless of the location of the injured spot, as shown in diagram I of Fig. 2. Actual curves have shown that, as illustrated in diagrams II and III, the rise of the pure monophasic curves either comes earlier or later than the initial deviation in unipolar-leg leads. When, however through imperfections of technique of leading, chiefly at the injury electrode, oscillations precede or are superimposed upon the ascending limb, their incidence is usually identical with that of the polarity changes at the injured spot as exemplified by the dotted line curves in diagrams II and III. In cases where records indicate the 2 rises as coinciding, the ascending limbs always possess these notches, as in diagram II. When the true monophasic curve

* There are theoretical objections to simultaneous leads from the same injured area.

actually begins ahead of the unipolar curve, the effects of this positivity under the injured electrode are seen on impure curves by a sudden sharp upward gradient on the ascending limb, depicted by the dotted oscillations in diagram III. If positivity and negativity should coincide at the rise, then this curve could still be looked upon to signify the incidence of negativity under the uninjured electrode lead.

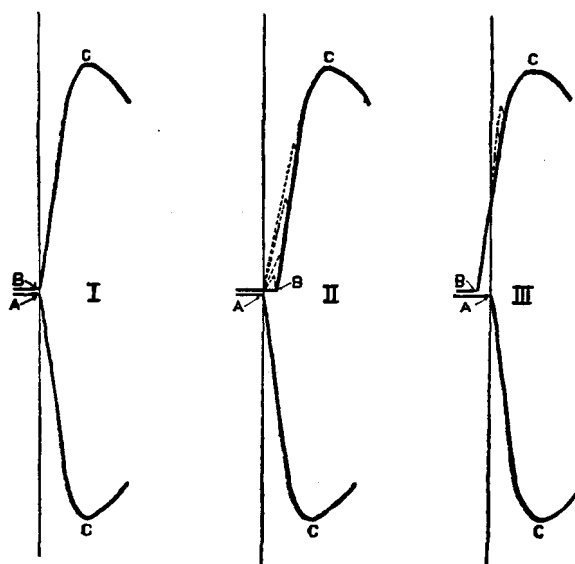


FIG. 2.

Three diagrams illustrating relations of pure and impure monophasic curve (upper) to unipolar leads from point of injury and left leg (lower). Discussion in text.

It is the second purpose to report that when pure monophasic curves are recorded from various points on the anterior and posterior surfaces of the ventricles, the point of injury being kept constant, then most points become negative at practically the same moment. This more nearly confirms the original descriptions of Erfmann⁴ and Clement⁵ than those subsequently, submitted by Lewis and Rothschild⁶ as a result of unipolar studies.

Attention is called to 3 interesting points: (1) A calculation of the maximum time-difference between the earliest and the most retarded appearance of negativity on the right and left heart in a series of 10 experiments, if the region overlying the interventricular

⁴ Erfmann, W., *Z. f. Biol.*, 1913, **61**, 155.

⁵ Clement, E., *Z. f. Biol.*, 1912, **58**, 110.

⁶ Lewis, T., and Rothschild, M. A., *Phil. Trans. Roy. Soc. London*, 1915, B 206, 181.

septum be excluded, reveals that in no case is this interval greater than 5 sigma, which is within the limit of the error of measurement. (2) The right ventricular surface receives its excitation only 5 sigma earlier than that of the left, the error of measurement having been taken into account. This time-difference is measured in sigma, not in hundredths of a second as were those of Lewis and Rothschild. (3) In over 80% of the cases, the epicardial surface overlying the interventricular septum apparently receives its excitation very definitely ahead of the remaining right and left myocardial surfaces, in some instances to the extent of 17.5 sigma.

The results now reported suggest that the impulses spread more rapidly than generally stated through the myocardial tissue so as to reach all points of the anterior and posterior surfaces practically simultaneously. A more thorough reinvestigation of the velocity as well as the spread of the cardiac impulses seems to be indicated.

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A Rat Test for Drug Addiction.*

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Further experiments on the addiction liability of various drugs in the albino rat have been carried out by the method previously described.¹ The test measures objectively progressive changes in the degree of irritability of the animal 24 hours after withdrawal of the drug throughout the period of administration. Advantage is thus taken of the most outstanding part of the abstinence syndrome clinically and experimentally, hyperirritability, to assess the ability of a drug to produce addiction.

The irritability of the rat which is normally fairly constant for a series of animals is quantitatively measured by determining the struggle response to a uniformly uncomfortable situation. Such a situation is provided by lashing the animal in the supine position to a small animal board so constructed that the animal is free to

* A part of this investigation has been made with the assistance of a grant from the Committee on Therapeutic Research, Council on Pharmacy and Chemistry, American Medical Association.

¹ Himmelsbach, Gerlach, Stanton, *J. Pharm. Exp. Therap.*, 1935, **53**, 179.