

October 28, 1969

Editor  
New England Journal of Medicine  
10 Shattuck Street  
Boston, Massachusetts 02115

Dear Sir:

Pitts and McClure (*N.Eng.Jour.Med.*, 1967, 277: 1329-1336) reported that intravenously administered sodium lactate precipitated a severe anxiety attack in 93% of individuals diagnosed as anxiety neurotics but in only 20% of normal controls. They were also able to minimize the effects of lactate by intravenous calcium.

We undertook a replication of this study, using their techniques and, with their cooperation, their lactate solutions. In five patients with lactate, each patient developed acute anxiety between the 8th to 12th minute of infusion, peaked at 15 minutes, and remained severe for 15 to 30 minutes. Each patient experienced "after effects" of irritability, dysphoria, tension, fatigue and weakness for 2-7 days.

The response to lactate/calcium was similar to lactate alone, but significantly less in intensity and duration; and there were no "after-effects". There was no patient response to dextrose/saline.

In four control subjects, the response to lactate was characterized by tachycardia and restlessness, but without anxiety in 3 subjects, nor "after effects" in four. Anxiety was elicited in one control. The controls became drowsy and bored with lactate/calcium and dextrose/saline.

As with Pitts and McClure, a "blind" investigator was able to correctly name 25/27 solutions (92.5%); the patients 13/15 solutions (87%); and the controls 6/12 solutions (50%).

In concurrent scalp recorded electroencephalograms, we observed changes with lactate in the patients, not shared by the controls or by dextrose/saline and lactate/calcium solutions. The EEG exhibited increased beta and decreased alpha abundances and a decreased alpha amplitude. These findings are consistent with the EEG changes usually seen in anxiety states.

Hypotheses relating anxiety and lactate are well summarized by Pitts and McClure. We would also add to their formulations that these observations have two interesting applications. A lactate tolerance test provides an objective means of identifying a group of mentally ill with common characteristics of anxiety neurosis, for both therapeutic and prognostic trials. The antagonism of calcium to lactate precipitated anxiety and its successful therapeutic trial (Pitts, personal communication) suggests that other anti-anxiety agents may be tested using this model.

Sincerely yours,

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Max Fink, M.D.

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Michael Alan Taylor, M.D.

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