

# T Wave Lability: A Clue For Separating The Good From The Bad, When Ugly

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## ABSTRACT

Non-specific T wave abnormalities have challenged both the clinician and the insurance medical director for decades. Distinction between pathologic and physiologic T wave changes often requires costly and time-consuming diagnostic studies. The literature is reviewed on the subject of T wave manipulation by the oral administration of both potassium and glucose, introducing the concept of T wave lability.

Based on this concept, a simple technique is suggested which, in many cases, can safely, expeditiously and inexpensively distinguish between organic and functional T wave changes. When employed in the investigation of asymptomatic insurance applicants with unexplained T wave abnormalities but no known cardiovascular or renal disease, this technique appears to be sufficiently reliable to classify the risk posed by non-specific T wave changes without resorting to a sophisticated, lengthy and costly cardiovascular investigation. [J INS MED 1996;28:79-85]

## INTRODUCTION

During the 1950's and 1960's, considerable attention was given to abnormalities of the electrocardiographic T wave and to the non-specificity of such T wave changes. An important outgrowth of interest on this subject was an increased awareness of the existence of functional T wave changes. Of particular note were the observations that (1) the ingestion of food or a measured quantity of glucose could reproduce functional T wave changes and (2) orally administered potassium could reverse such changes.<sup>1</sup>

The phenomena of glucose- and potassium-induced alteration of the T wave have meaningful diagnostic implications — both clinically and in the area of insurance risk classification. A better under-

standing of this concept may be derived from a review of the various causes of T wave changes, the implications of their non-specificity, known facts regarding cardiac electrophysiology, and the results of prior studies on the EKG effects of oral potassium and glucose.

## Classification of T wave Changes

In his classic 1953 article on the non-specificity of electrocardiographic changes, Harold Levine listed 67 factors affecting the T wave of the EKG and declared the list to be "very incomplete."<sup>2</sup> Forty-three years later that list is still pertinent and inclusive of most causes of T wave abnormalities.

In addition to myocardial ischemia and anoxia, Levine's etiologic classification of T wave abnormalities recognized a diversity of non-cardiac factors, including both pathologic and physiologic conditions. More recently, the medical literature has made the distinction between primary and secondary T wave changes.<sup>3</sup> Primary T wave changes are, by far, the largest and most diverse category of T wave abnormalities and are due to altered myocardial cellular metabolism arising from numerous physiologic and pathologic conditions (both cardiac and extracardiac), directly affecting repolarization. Secondary T wave changes are those which are merely obligatory to preceding depolarization abnormalities, such as LBBB. The polarity of these secondary T waves is generally the same as the direction of the terminal portion of the abnormal QRS deflection.

Various classifications of electrocardiographic T wave abnormalities have been proposed over the years.<sup>3,4,5,6</sup> Table 1 represents a hybridism of these earlier classifications and should be helpful to the underwriter in contemplating the differential diagnosis of abnormalities of the electrocardiographic T wave.

**The non-specificity of T wave changes**

This brings us to a consideration of what is meant by the recurring term "non-specific T wave changes". It has been observed that the T wave abnormalities of myocardial ischemia have a characteristic appearance: symmetric inversion — suggesting that such a configuration is "specific" for ischemia. However, there are significant exceptions to that tenet. As an example, based on the EKG alone, there really is no means of distinguishing the T wave changes of anteroseptal myocardial ischemia from those seen in the presence of partial persistence of the juvenile precordial pattern (a normal variant).

Actually, the commanding majority of primary T wave changes would remain non-specific in the absence of correlation with the medical history. In one large series of 410 EKG's exhibiting ST segment and/or T wave abnormalities, 70% were interpreted as "non-specific STT changes" when no clinical data were provided, while only 10% were seen as non-specific when the pertinent history was reviewed.<sup>7</sup>

ST segment and T wave changes are the most common EKG abnormalities, and it has been estimated that non-specific T wave changes are encountered in 3.5% of all routine EKG's.<sup>8</sup> Furthermore, these T wave alterations are the least specific of all EKG changes. Assessment of non-specific T wave abnormalities has long been an enigma to the electrocardiographer, and such changes are subject to the greatest misinterpretation. The unfortunate consequences of these uncertainties exist as two extremes: (1) complacency and failure to address a significant medical condition when the findings are downplayed as inconsequential and (2) unjustified emotional disablement when over-interpretation has led to mislabeling the patient.

In insurance risk classification those same two extremes can lead to either (1) acceptance of substantially impaired risks at standard rates or (2) denial of insurance on individuals whose EKG's are altered by innocent physiologic influences. Such inaccuracies can be minimized by improved selectivity. This will be discussed below.

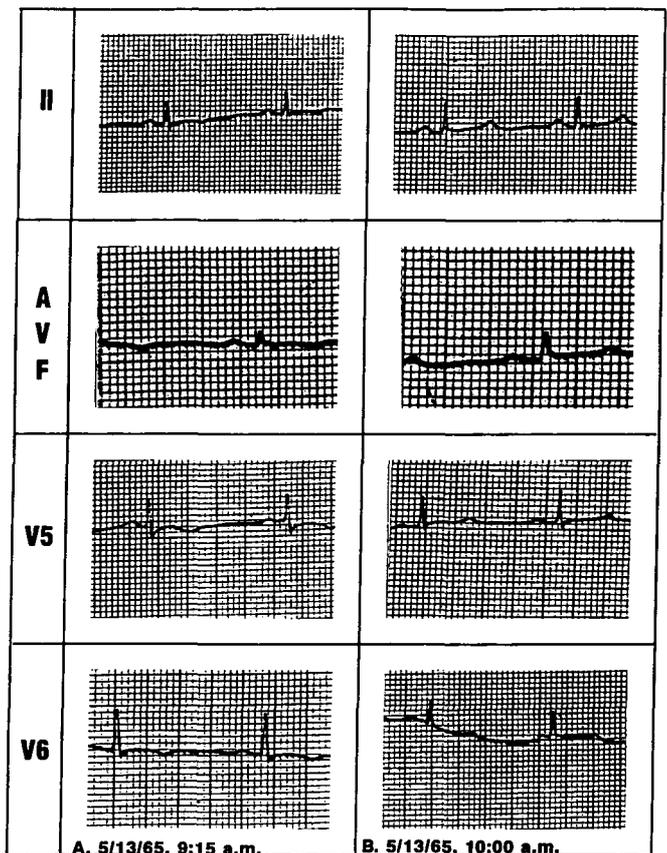
**Case History: I**

On May 13, 1965, an asymptomatic 47 year old male with no significant medical history was evaluated by this author in an attempt to explain previously demonstrated abnormalities of his electrocardiographic T waves. A baseline EKG (Figure 1A) revealed flat to

inverted T waves in the anterolateral and inferior leads (similar to the prior abnormalities exhibited by the subject in both the fasting and non-fasting states). The patient was then administered an oral dose of 100 mEq (3,912 mg) of potassium (supplied by 10 g of potassium bicarbonate). Following a 45 minutes rest period, a repeat EKG exhibited complete resolution of the T wave abnormalities (Figure 1B). During a ten year follow up the patient developed no cardiovascular history and had repeatedly negative routine annual treadmill stress tests.

**Case History: II**

On March 13, 1995, a healthy 40 year old male underwriter was found to have major T wave changes during a routine insurance examination while fasting. Arrangements were then made for repeat electrocardiography with special instructions to perform a baseline resting EKG followed by the oral administration of 100 mEq potassium (in the form of four effervescent tablets of potassium bicarbonate) and repeat electrocardiography after a 45 minute period of rest. Major T wave changes were again recorded on the baseline

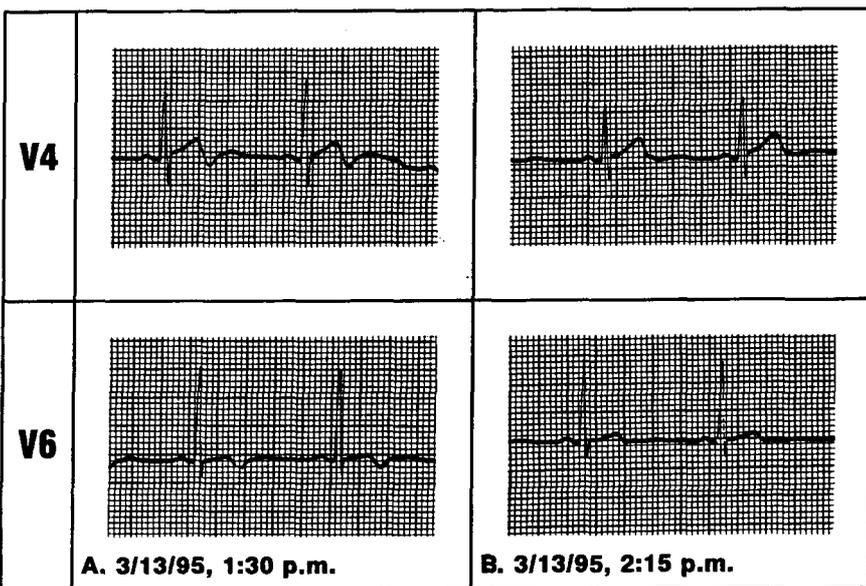


**Figure 1. Effect of Potassium on Non-specific T Wave Changes.**  
 A, Baseline Non-fasting EKG. B, Forty-five Minutes After Oral Potassium (100mEq).

EKG (Figure 2A), and reversal of these changes occurred after ingestion of the potassium. (Figure 2B). A subsequent maximal treadmill stress test was entirely normal, exhibiting no ischemic changes.

**The Potassium Connection**

The T wave of the electrocardiogram is the result of ventricular repolarization — the recovery phase of the cardiac cycle, in which the resting membrane potential of the ventricular myocardial cells is restored. In this polarized state, the inside of the cell membrane changes from positively charged to negatively charged, while the outside of the membrane reverts from a negative charge to a positive charge. Complex processes are responsible for this phenomenon, and one of the more important factors involves



**Figure 2. Potassium-loading EKG: Demonstrating T Wave Lability.** A, Baseline Non-fasting EKG. B, Forty-five Minutes After Oral Potassium (100mEq).

the efflux of positively charged potassium ions via potassium channels from the interior to the exterior of the cells.<sup>9</sup>

This electrophysiologic phenomenon is the basis for observations described by Ferrer in the Summer 1995 issue of J.I.M. — namely that functional T wave changes may occur during the post-absorptive state through the mechanism of a shift of potassium out of the serum.<sup>10</sup> This circumstance can account for the appearance of non-specific T wave abnormalities among a number of resting EKG's. Hence, the wisdom of Ferrer's advice to obtain repeat EKG's in the fasting state whenever possible. If this repeat electrocardio-

gram is normal, it can justifiably be concluded that the original T wave changes were possibly functional and merely due to the non-fasting state. The obvious benefit of this technique is the avoidance of a complex diagnostic work-up.

However, functional T wave changes may occur independent of food intake<sup>1</sup>. The innocent nature of such changes cannot be revealed by fasting electrocardiography alone. This circumstance often triggers an extensive cardiovascular investigation, when a simpler approach (described below) could achieve comparable diagnostic accuracy.

In the late 1950's and early 1960's, interest developed in studying the influence of orally administered potassium on electrocardiographic T wave abnormalities. Although the literature is unclear on this point, that interest was likely stimulated by recognition of (1) the connection between normal ventricular repolariza-

tion and the above-described extracellular shift of potassium and (2) the long recognized association between hypokalemia (a functional alteration) and T wave abnormalities. The information derived from these studies is noteworthy.

**Results of Potassium Loading trials: "T Wave Lability"**

A number of clinical studies between the early 1940's and the late 1960's addressed the effects of orally administered potassium on ventricular repolarization and T wave configuration. While there is no prior indication of such terminology in the medical literature, this technique will now be referred to as potassium-loading electrocardiography (K-loading EKG).

Some of these studies produced striking evidence of the ability of oral potassium to differentiate organic from functional T wave changes.<sup>11,12,13,14</sup> Other investigations challenged such findings.<sup>15,16,17</sup>

Still other reports pointed to a substantial incidence of toxicity to the administered potassium<sup>11,13</sup>, but this has been attributed to excessive dosage (in the range of 200-300 mEq) and/or administration of potassium to individuals with advanced cardiac and/or renal disease.<sup>18</sup> Uncommon adverse reactions included nausea, vomiting, epigastric burning, paresthesiae, sinus tachycardia, ventricular ectopic activity, conduction disturbances and AV nodal rhythm.<sup>11,13</sup>

Four separate K-loading EKG studies between 1958 and 1969<sup>12,13,14,18</sup> separated 304 subjects into those who had unequivocal evidence of organic heart disease and those with no evidence of heart disease, based on history, physical examination and laboratory data, exclusive of electrocardiography. Subjects in these two subsets were administered 200-250 mEq of oral potassium after baseline EKG's and the tracings were repeated at intervals of 1-2 hours following the potassium load. Among the 179 subjects with heart disease and baseline non-specific T wave changes, the abnormalities persisted in 166 (93%). On the other hand, 125 of 125 subjects without heart disease but with baseline non-specific T wave changes exhibited normalization or near normalization of their T waves. (One study also identified eight subjects who, at baseline, were both clinically and electrocardiographically normal and in whom the potassium load had no effect on the EKG.)

Out of these studies the concept of T wave lability evolved. In short, this term refers to the inclination of some non-specific T wave changes to undergo substantial transient alteration in response to simple, physiologic provocations. Such stimuli include changes in body position, altered breathing and the ingestion of potassium or glucose. The implication of this T wave lability (or "fickleness") is that its presence identifies non-specific T wave changes which are most likely not representative of organic heart disease. Additionally, elicitation of labile T wave changes during the baseline EKG prior to stress testing (by standing and/or hyperventilation) gives support to an opinion that any ensuing exercise-related ST/T changes may be representative of a false positive result.

The demonstration of *T wave lability* by K-loading EKG does not rely on the presence of hypokalemia or its correction. The phenomena of functional non-specific T wave changes and their reversal by potassium ingestion are fully operative in the normokalemic state.<sup>1</sup>

### Case History: III

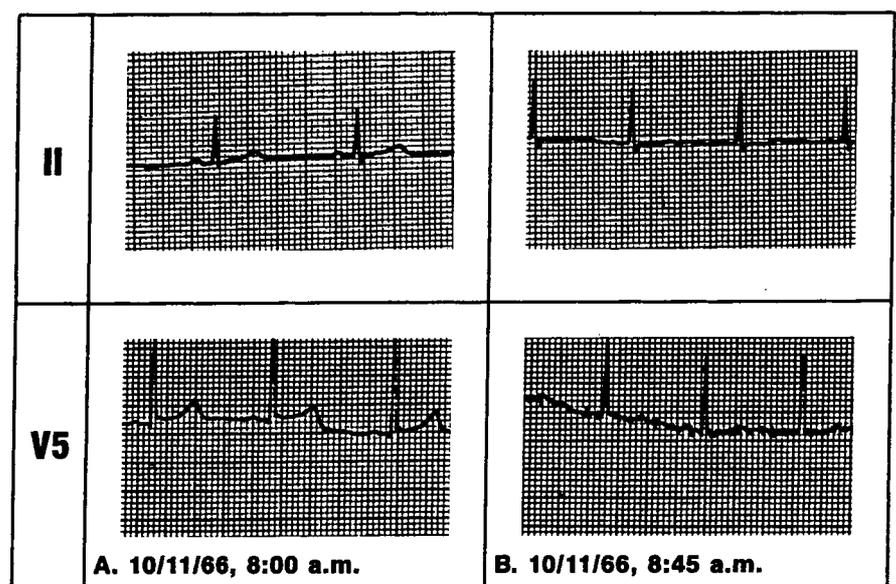
On October 11, 1966, an apparently healthy 21 year old female was seen in consultation by this author for evaluation of previously observed non-specific T wave changes, unrelated to the ingestion

of food. The baseline tracing (Figure 3A), showing only early repolarization, was conducted during the fasting state, after which the patient ingested an oral solution of 75 g of glucose (as used in the standard oral glucose tolerance test). A repeat EKG 45 minutes later (Figure 3B) revealed diffuse non-specific T wave changes which were identical to those seen intermittently during the recent past. On the basis of this test result, it was concluded that the prior T wave changes were probably functional and of no clinical significance. Justification of the assurance given this patient at that time has been borne out by her subsequent accomplishments as an amateur tennis champion and by the uneventful delivery of her four children.

### The Glucose Connection

The ingestion of glucose has rather complex effects on the shift of potassium between extracellular and intracellular compartments. As a consequence of the transient increase in serum osmolality following intestinal absorption of glucose, there occurs a transfer of intracellular water to the extracellular fluid. This is accompanied by a shift of potassium to the extracellular fluid as the result of both (1) "solvent drag" in which the solute ( $K^+$ ) is carried along with the solvent (water) as it exits the intracellular space, and (2) an increased intracellular:extracellular potassium concentration gradient which favors passive exit of potassium from the cells into the extracellular fluid.<sup>19</sup>

However, this is more than offset by the insulin response to a transient increase in blood glucose.



**Figure 3. Effect of Glucose on the T Wave.** A, Baseline Fasting EKG. B, Forty-five Minutes After Oral Glucose (75g).

Insulin stimulates the enzyme sodium-potassium-adenosine triphosphatase (Na-K-ATPase) activity which catalyzes the sodium-potassium pump, resulting in increased entry of potassium into the intracellular space, mainly involving skeletal muscle and the liver. The net effect is a temporary reduction in extracellular potassium, resulting in an increase in the transmembrane resting potential of myocardial cells.<sup>19,20</sup> This mechanism, as noted above, has been implicated in the genesis of post-absorptive functional T wave changes,<sup>10</sup> and it serves as a tenable explanation for the glucose-induced T wave changes in Case History III, above.

## Methodology

Case Histories I, II, and III illustrate the application of a precise protocol for identifying the presence or absence of T wave lability, thereby providing evidence which can be helpful in making the distinction between organic and functional causes of T wave changes. That technique may be indicated in the presence of previously detected unexplained non-specific T wave changes in subjects with no clear cardiovascular history or renal insufficiency. It should be conducted only by the attending physician — who should be informed of the purpose, physiologic basis and rationale for this test. The protocol may be expressed as follows:

### K-loading (or Glucose Challenge) EKG<sup>i</sup>

- A. Baseline 12-lead EKG.
- B. Proceed on the basis of the baseline EKG interpretation:
  1. Normal T waves: challenge with oral glucose.
  2. Abnormal T waves: challenge with oral potassium.
- C. Immediately after the baseline EKG: If T wave abnormalities are present, orally administer 100 mEq of a potassium supplement<sup>ii</sup> dissolved in iced water or juice over a five minute period. (Alternatively, if the baseline T waves are normal, orally administer 75g of glucose in an iced solution<sup>iii</sup> over a five minute period.)
- D. Rest period.
- E. Repeat EKG in 45-90 minutes. (Optimal time interval will vary from individual to individual.)

### F. Interpretation:

1. Potassium challenge
    - a. Normalization of previously abnormal T waves in at least 2 leads: positive for T wave lability and probably indicative of a functional/physiologic basis for the original T wave changes.
    - b. Lesser or no reversal of T wave abnormalities: negative for T wave lability, with an increased likelihood that the T wave changes have an organic basis.
  2. Glucose challenge:
    - a. T waves remain normal: negative for T wave lability, therefore inconclusive, but suggestive that prior T wave changes may have been pathologic.
    - b. Reproduction of prior T wave changes: positive for T wave lability, pointing to the strong likelihood that prior T wave abnormalities were functional/physiologic.
- i. If prior EKG's are predictive of an abnormal insurance EKG, this protocol may be employed as a contingency at the time of the original insurance EKG, thereby avoiding repeat evaluation with its inconvenience and added acquisition costs.
  - ii Suggestion: K-Lyte® Effervescent Tablets, 50 mEq (3,730 mg), 2 tablets (orange or lime flavor) dissolved in cold water.
  - iii Suggestion: Glucola, as used for an oral glucose tolerance test.

## Discussion

Two curiosities surrounding the K-loading EKG findings are the paucity of further investigation after the late 1960's and the failure to exploit the observed phenomenon by using it to enhance the diagnostic capability of resting electrocardiography. Perhaps the lack of absolute certainty in the interpretation of K-loading or glucose challenge EKG results and the advent of highly sophisticated (and very expensive) cardiovascular diagnostic technology combined to assure the technique an early grave.

However, while clinical medicine, with its penchant for verifiability, may have little use for K-loading/glucose challenge EKG's (a position which should be questioned), risk classification for insurance purposes relies on probabilities rather than certainties — meaning that the goal of insurance risk assessment is attained by achieving less than complete accuracy. Given this precept and the need to secure underwriting evidence by means which are minimally obtrusive to the proposed insured and maximally cost-effective, a strong case can be made for the selective use of the

K-loading/glucose challenge EKG as an underwriting tool.

The obvious applicability of K-loading EKG's to the underwriting process is in the resolution of that uncertainty which accompanies the detection of minor or major non-specific T wave changes in the resting EKG of an asymptomatic adult. In this setting repeat resting electrocardiography before and after a potassium load can be easily accomplished. If the T wave changes disappear after the potassium load, it would seem prudent, based on the revelations of the 1960's, to conclude that the changes are almost certainly non-organic and not predictive of extra mortality or morbidity. Accordingly, stress testing (and its relatively high cost) could be avoided and a standard offer of insurance could be made with no further investigation. If, on the other hand, the T wave changes persist after potassium loading, significant heart disease should be suspected, and this unresponsiveness of T wave abnormality to oral potassium should permit a clearer underwriting decision to either conclude that organic heart disease may be present or require further testing or consultation.

Although less perplexing, another EKG finding of concern is the prior observation of T wave changes but a normal pattern at the time of the insurance exam. Again, demonstration of T wave lability can detract from the significance of the earlier abnormalities. When the T waves have reverted to normal at the time of the exam, this lability can be uncovered if the T wave abnormality is reproduced by a simple physiologic manipulation such as assumption of the upright position, hyperventilation or drinking cold water. Actually, the preferred technique in this regard is carbohydrate ingestion as employed in Case History III. The physiologic basis for this form of challenge and the methodology are discussed above. In interpreting the results of the challenge, reproduction of the T wave changes should mitigate against the significance of the abnormality, while non-reproduction of such changes should be interpreted as an inconclusive result.

## Conclusions and Recommendations

It has been clearly demonstrated that the electrocardiographic response to oral potassium loading or glucose challenge is an effective and practical means of discriminating between organic and functional T wave changes. Studies which established this relationship largely date back to the 1960's, but the observation remains fully operative today, as illustrated by the previously cited Case History: II.

K-loading/glucose challenge EKG testing techniques are safe procedures when employed only for the investigation of non-specific T wave changes in otherwise apparently normal adults and when the dosage is limited to 100 mEq of potassium.

In our experience the cost of this technique is approximately 1/3 that of a treadmill stress test.

The phenomenon of T wave lability and its tendency to create the false impression of organic heart disease (and unnecessarily adverse underwriting decisions) can be minimized through the following measures (for both resting EKG's and stress testing):

1. Overnight fasting prior to electrocardiography.
2. Avoid diuretics for 4-6 days (with the attending physician's approval).
3. Correct hypokalemia if present (under the supervision of the attending physician).
4. K-loading or Glucose Challenge EKG Testing, as described above (Methodology). Most attending physicians and special examiners (whose cooperation will be necessary in executing this investigation) will be unfamiliar with this approach, but any resistance to the performance of the test should be diffused by the insurer's explanation of the basis for the test, its safety and its potential benefit to the patient/proposed insured.

## Acknowledgement

The author is indebted to his original cardiology mentor, Dr. Charles Fisch who, as a professor of medicine at the Indiana University School of Medicine over thirty years ago, first planted the seeds of the concept introduced in this article. Dr. Fisch is a past president of the American College of Cardiology and served as Director of the Krannert Institute of Cardiology until 1990. His numerous publications on electrocardiography and cardiac electrophysiology, and his willingness to discuss the phenomenon of T wave lability with the author have been valuable in the contemplation of the subject presented in this article.

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