Similarity and Difference in the Electrocardiogram between Actual Neurosis and Hyperthyroidism with Special Reference to the U Wave*

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Being encouraged by the statistical results of the previous report on U wave changes in patients with neurogenic cardiac complaints, the author investigated the similarity and difference in ECG between actual neurosis (Aktualnurose) and hyperthyroidism. It seemed to the author that there may be a borderline case between actual neurosis and hyperthyroidism as there is a borderline hypertension between normotension and hypertension, and that an analysis of clinical records might add something to our knowledge of the causation of the U wave.

As to the pathogenesis of hyperthyroidism, HILL and Selenkow stated that "In a large number of cases there is a clue in the correlation between episodes of psychic trauma, infections, injury, or other types of stress at the onset of thyrotoxicosis". REINWEIN also stated that "Die ersten Erscheinungen können manchmal stürmisch, im Anschluß an eine psychische Erregung oder an eine andere Erkrankung, auftreten. Als auslösende Ursache spielen wahr- scheinlich außerdem die Infekte eine Rolle, weil sie das endokrin-vegetative System belasten und den Stoffwechsel steigern. Da aber nicht jede Person, die Infekte durchmacht oder ein schweres seelisches Ergebnis hatte, später ein Basedowleiden bekommt, ist anzunehmen, daß die prämorbid Persönlichkeit von richtunggebender Bedeutung ist". FREYSCHMIDT is of the opinion that "Auf die TSH-Inkretion nehmen höher gelegene Zentren im Hypothalamus Einfluß, welche wiederum Impulse von der Großhirnrinde empfangen können... Da über die Zentren des Hypothalamus noch eine enge Ver-

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The outlines of this paper were read before the 17th Tokai regional meeting of Japanese Circulation Society on November 30, 1963.

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plaints in this decade. A complete disappearance of the U wave in patients with neurogenic cardiac complaints tended to extend from the left to the right precordial leads up to V₂ with continuation of stressful life. The U wave in patients with organic cardiac complaints tended to increase in height up to 3.0 mm especially in the right precordial leads, unless ST depression was marked. Usually, a flattened or negative U wave followed a marked ST depression and a flattened or inverted T wave. The presence of a distinct U wave in V₄ and V₅ in patients with diverse, rambling complaints usually indicated the presence of the lability of the autonomic nervous system, talkative or hysterical character or a fear of a certain disease with a shorter than 1 month duration. The characteristics of the concrete contents of mental conflict or emotional tension drawn out on the basis of the ECG changes from patients with neurogenic cardiac complaints were that the stress had continued for more than 1 month before the 1st consultation and that there is no prospect of its resolution in the near future.

It was not the purpose of this paper to determine the mechanism by which U wave changes are produced but rather to estimate its clinical significance. It seemed to the author, however, that an analysis of clinical records might add something to our knowledge of the causation of the U wave.

As shown in the previous report "neurosis" we encounter most often in outpatients is "Aktualneurose" of Boss⁵ or "neurasthenic states" of SADLER in which fatigue neurosis, anxiety neurosis, sexual neurosis, occupational neurosis, hypochondria and neurasthenia are included. It was felt that there may be a borderline case between neurosis and hyperthyroidism just as there is a borderline hypertension between normotension and hypertension and there is subdiabetes between non-diabetes and diabetes mellitus. "Actual neurosis" employed in this paper comprises all of those disturbances not only in the autonomic nervous system but also in the mental equilibrium which are caused by stresses of any kind, occupational, domestic, emotional, bodily or sexual. Hystera and psychoneurosis in a strict sense which are dealt with in deep psychology are not included.

MATERIALS AND METHODS

In 17 patients the BMR was measured with a Sanborn metabolator, and 10 of them had a BMR higher than +15%. In a group of actual neurosis, 24 patients from whom concrete contents of the mental conflict was drawn out were selected. As the control 20 healthy individuals were employed. After the 17th Tokai regional meeting of Japanese Circulation Society on November 30, 1963, 4 patients with hyperthyroidism and 4 patients with actual neurosis were added to this report to give typical examples of the course of ECG changes, but the statistical data were left unchanged as read before the meeting. Those patients who had cardiac failure on the 1st consultation day were not included and those who showed one or more of the following findings were excluded: a pulse rate of more than 100/min, essential hypertension, bundle branch block or atrio-ventricular block. However, those with supraventricular and ventricular premature contractions which both come not infrequently in patients with actual neurosis were not excluded. The QT interval (in case of a complete U wave disappearance it may actually be the QU interval) and the height of the T and R waves were measured in V₅. The QT ratio was obtained from the nomogram of Goldberger⁶, and the T/R ratio was calculated. The measurement of the U wave was the same as previously reported. Namely, when no U wave followed the T wave it was scored as 0. When 1 to 2 traces of the U wave followed 1 to 2 of 4 T waves or when the downstroke of the T wave fused stepwise into the U wave, it was scored as 0.5. When 4 T waves were followed with 4 distinct U waves lower than 0.5 mm or with the U wave with a height of 0.5 to 3.0 mm, it was scored as 1. A negative U wave was not observed in this survey.

RESULTS

1) ECG in hyperthyroidism

As shown in Fig. 1, ECG in patients with hyperthyroidism without congestive heart failure showed the following characteristics: a shortened RR interval, an elevated, normal or depressed concave ST segment in V₄, V₅ and V₆, a slightly to moderately depressed T wave with a characteristically blunt, round turning point, an increase in the QT ratio, and a complete disappearance of the U wave in V₄, V₅ and V₆.

2) ECG in actual neurosis

As shown in Fig. 2, ECG in patients with actual neurosis with pure heart sound and with normotension or borderline hypertension showed

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the following characteristics: a normal RR interval, a slightly to moderately elevated concave ST segment in V5 and V6, a heightened T wave with a characteristically tapering, peaked turning point in V5 and V6, a normal QT ratio and a depressed U wave in V5 and a complete disappearance of the U wave in V5 and V6.

3) ECG in patients with symptomatically similar pictures

As previously reported, ECG in patients with the lability of the autonomic nervous system, hysteria or with a fear of a certain disease with a shorter than 1 month duration showed a normal U wave in V4 and V5. For the past 6 months the writer experienced 2 cases of schizophrenia, and both of them showed a normal U wave in the precordial leads.

4) The percentage of U wave appearance in unipolar precordial leads in hyperthyroidism and actual neurosis

As shown in Fig. 3, the percentage of the U wave appearance in the left precordial leads in both hyperthyroidism and actual neurosis was strikingly low as compared to that of controls. Namely, in hyperthyroidism it was 20% in V4 and 0% in V5 and V6. In actual neurosis it was 25% in V4, 2% in V5 and 0% in V6. In controls it was 95% in V4, 85% in V5 and 35% in V6.

5) The QT ratio in V5

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1) Y. T. ∙ 52 Years Old, Blood Pressure: 130/80 mmHg

2) S. T. ∙ 30 Years Old, Blood Pressure: 140/86 mmHg

3) I. Y. ∙ 28 Years Old, Blood Pressure: 150/90 mmHg

4) S. B. ∙ 49 Years Old, Blood Pressure: 120/80 mmHg

5) S. S. ∙ 40 Years Old, Blood Pressure: 128/82 mmHg

Fig. 2. ECG in Actual Neurosis

As shown in Table I, there was no significant difference in the QT ratio between patients with actual neurosis and control subjects, i.e., it averaged 1.04 in the former and 1.01 in the latter. However, it was markedly increased in patients with hyperthyroidism up to 1.23.

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<th>Table I: The QT Ratio in V₅</th>
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<td>Actual Neurosis</td>
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6) The T/R ratio in V₅

As shown in Table II, there was no significant difference in the T/R ratio between actual neurosis and controls, i.e., it averaged 0.40 in the former and 0.37 in the latter. However, it was markedly lowered in hyperthyroidism down to 0.17.

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<th>Table II: The T/R Ratio in V₅</th>
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7) Relation between the QT ratio and the basal metabolic rate

The BMR was measured not later than 2 days.

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after ECG registration. As shown in Fig. 4, there was a direct correlation between the two. All of these data were those obtained before treatment from different cases.

8) Changes in ECG in hyperthyroidism after treatment

As shown in Figs. 5 and 6, the ECG characteristics in hyperthyroidism were lost with a lowering of the BMR, and the characteristic ECG patterns of actual neurosis appeared. And further, with a continuation of euthyroidism for more than 6 months produced a normal U wave in V5 as shown in Fig. 7. In a patient with a large struma in which methimazole administration was discontinued for the preparation of surgical treatment, the ECG returned from the pattern of actual neurosis to that of hyperthyroidism as shown in Fig. 8. In a case of the feed back phenomenon which appeared after 3 weeks of methimazole administration, the ECG showed similar changes to those observed in the case of methimazole-discontinuation as shown in Fig. 9.

9) Changes in ECG in actual neurosis after treatment

Usually, it is only a small percent of cases of actual neurosis in which the course can electrocardiographically be followed up because subjective improvement can relatively be easily obtained by a tranquilizer and psychotherapy.

As previously reported, the concrete contents of mental conflict or stress can be drawn out from nearly all patients on the basis of ECG changes. Fig. 10 shows one of a few cases in which an
electrocardiographic follow-up was unexpectedly made. On the 1st consultation day the patient complained of palpitation and tightness of the chest and was told by a doctor that he had angina pectoris and that he might have a fatal myocardial infarction unless he took an absolute bed rest. He is a tailor and had too many contracts with deadlines at the year end. He cancelled all the contracts and took an absolute bed rest but more frequently palpitation occurred at night and the tightness of the chest continued. One day he happened to be examined by the writer and was told that there was neither sign of coronary insufficiency nor indication that he might have heart attack. Further, he was encouraged to leave his bed, move and go back to his business. On that day he spoke out not only occupational but also domestic affairs. He has 4 sons, the eldest one being 36 years of age, still unmarried, and none of them took over his business. The ECG recorded about a month later (Fig. 10–d) was almost normal with a distinct U wave in V5.

10) Serum potassium in actual neurosis

Serum potassium concentration determined in 10 patients with the characteristic ECG pattern of actual neurosis averaged 4.13 mEq/L, ranging from 3.7 to 4.8 mEq/L.

**DISCUSSION**

1) The U wave
As to the origin of the U wave, Einthoven

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stated as follows: “Ein bedeutender Teil des Herzens kann schon in den Erschlaffungszustand übergegangen sein, so daß der Druck in den Kammerhöhlen so gut wie ganz verloren gegangen ist, während doch noch einige Fasern sich im Kontrakptionszustand befinden. Erst wenn diese letzteren vollständig erschlafft sind, hat die U-Zacke ihr Ende erreicht”. On the basis of his fundamental experiment on ECG, MAEKAWA is of the opinion that “During the spreading of the contraction-wave, coming from the auriculo-ventricular junctional tissue over the whole of the ventricles, the QRS group is inscribed... But this does not mean that at this moment all the ventricular fibres have become involved as EINTHOVEN and other authors believe, because the contraction waves show that at this moment and even after this moment these are still developing... The ST interval, being thus described the contraction spreads further to all the ventricular fibres, and when it reaches its maximum development the T wave also reaches
a) October 7, 1963, BMR: +30%, Blood Pressure: 120/80 mmHg, QT Ratio: 1.05

b) November 8, 1963, BMR: +41%, Blood Pressure: 146/60 mmHg, QT Ratio: 1.06

c) November 19, 1963, BMR: +57%, Blood Pressure: 140/60 mmHg, QT Ratio: 1.15

d) November 26, 1963, BMR: +68%, Blood Pressure: 130/60 mmHg, QT Ratio: 1.17

Fig. 8. Changes in ECG after Methimazole Discontinuation T. U. 5 35 Years Old

its peak... After the full development of the systole, the ventricular muscles begin to relax. During the spreading of this relaxation to most of the ventricular muscles, the downstroke of the positive T wave is inscribed, just as during the spreading of the contraction the QRS group is inscribed. But all the ventricular fibres do not become involved in the relaxation at the end of the T wave. The end of the T wave comes in a very early phase of the relaxing portion of the upper and the lower contraction curves. Thus the spreading of the ventricular relaxation after the end of the T wave is represented by the electrical expression as a U wave". MAEKAWA further stated that "If all parts of the ventricles relax equally at the same time, the U wave does not appear in the ECG". From his principle which shows that the U wave (b') in the diastole is the counterpart of the ST-segment and the upstroke of the T wave (b) in the systole and that the downstroke of the T wave in the diastole (a') that of the QRS complex in the systole (a), it is natural that changes in the U wave are almost always accompanied by changes in the ST-segment. Normally, a/b = a'/b' = 1/2.5 and a'/b = b'/b = 1/1.4. LEPESCHKIN stated that "If the potential across the cell membrane is decreased to about 60 mV, either by an external stimulating current or by the action potential of a neighbouring cell, the sodium permeability of the cell membrane increases greatly. As the concentration of the positively charged sodium ions is at least 10 times as great outside as inside the cell, this..."
causes large amounts of these ions to enter the cell, so that the inside now suddenly becomes about 20 millivolts more positive than the outside. Potential differences during this steep ascent of the trans-membrane action potential are responsible for the QRS complex of the electrocardiogram. Return to normal of the increased sodium permeability causes the positive intracellular potential to decline to zero. In the specific conducting system this return is rapid, causing a large rapidly descending spike of the action potential. . . The decrease of sodium permeability permits diffusion of the positively charged potassium ions out of the cell to slowly start restoring the resting membrane potential, causing the initial slow portion of the descending branch of the action potential (plateau).

The accumulation of potassium ions on the outside of the cell membrane during repolarization apparently causes a progressive increase in potassium permeability, so that the terminal portion of the descending branch becomes steeper and steeper. . . At the end of the action potential repolarization again becomes slower since the potassium gradient across the cell membrane decreases due to further accumulation of potassium ions outside of the membrane; this delayed complete repolarisation may cause a low after-potential. The slow initial descending branch of the action potential is responsible for the ST-segment of the electrocardiogram, the rapid terminal branch for the T wave, while the after-potential is at least partly responsible for the U wave". He stated also thet "If the external

Fig. 9. Changes in ECG in the Feed Back Phenomenon K. C. ° 20 Years Old

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potassium is high, less potassium can be expected to leave the cell and more will be reabsorbed during diastole; the negative after-potentials can therefore be expected to become smaller". Namely, according to Lepeschkin, an increase in the sodium permeability is responsible for the QRS complex and that in the potassium permeability for the T wave. As to the fusion between T and U waves, Holzmann\textsuperscript{12} stated that "accurate identification of the U wave is also needed for a correct determination of the QT duration. This identification is sometimes difficult because of superposition and fusion of the T and U waves. The term superposition is applied to patterns in which these waves are only partially merged and a notch is present by which the 2 components can be separated. The term fusion implies uniform monophasic or diphasic waves that show no landmarks for the differentiation of their components". He demonstrated 48 theoretical patterns that can result from different degrees and types of merging of T waves of different heights with different forms of U waves. However, in his theoretical patterns an isoelectric U wave was not taken into consideration. More practically, he classified the fusion between T and U waves into 3; 1) TU-fusion wave with a summation apex, 2) TU-fusion wave with predominance of T and 3) TU-fusion wave with predominance of U. These theories based on fundamental, experimental data or on theoretical reasoning clarified some of the most important aspects of ECG. However, the human heart is under the control of the autonomic nervous and the endocrine systems, and these are subjected to the emotional tension or mental.

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conflict, which is absolutely human.

2) U wave disappearance

Three representative types of U wave disappearance will be given below: Fig. 11 can be explained by the MAEKAWA principle; an elevated concave ST-segment in V4 and V5 associated with an isoelectric U wave turned out to be an isoelectric ST-segment associated with a distinct, positive U wave after exercise. The patient was promoted to a superintendent with an unbearable responsibility about 2 months before the 1st consultation. His chief complaints were insomnia, palpitation at night and malaise. Fig. 12 can be explained by Holzmann's theory; a TU-fusion wave with predominance of T returned to normal after 1 month's hospitalization. The patient, a man of influence in his town, failed in his enterprise and attempted suicide after 3 weeks of disappointment and insomnia before admission. Fig. 13 may be a TU-fusion wave with a summation apex. After 3 month's hospitalization, a normal U wave appeared without significant changes in the ST-segment and the T wave. Taking Lepeschkin's theory into consideration, changes in the intra/extracellular potassium gradient may be responsible for this change. It was revealed that the wife of this patient manages a hotel but the patient himself spent the past 20 years in having a game of "go" making money by speculation. About 6 months before the 1st consultation he failed in speculation and lost 1 million yen. On the 1st

S. M. 5 43 Years Old, Blood Pressure: 140/90 mmHg, March 13, 1963
a) before exercise

b) after exercise

Fig. 11. Normalization of ST Elevation in V4 and Reappearance of the U Wave in V5 after Exercise

M. I. 5 67 Years Old
a) June 1, 1963, Blood Pressure: 120/80 mmHg

b) July 11, 1963, Blood Pressure: 140/80 mmHg

Fig. 12. Reappearance of the U Wave in a Neurasthenic Patient after 1 Month of Hospitalization

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consultation day he said that he had hemiplegia for the past 6 months. Actually, he could not walk by himself on that day, but there was no pathological reflex. He walked by himself from the 3rd hospitalization day after he confided everything to the attending doctor.

3) Concave RS-T elevation

Fenichel\(^{19}\) published a report entitled "A long term study of concave RS-T elevation—A normal variant of the electrocardiogram". He described that "The electrocardiograms of 82 patients, or 6.7% of the entire series, showed a concave RS-T elevation in one or more leads. Seventy-five of these patients had apparently normal heart, whereas the other seven, or less than 9% of the group revealing this shift, had clinical heart disease. In the normal group there was a great preponderance of men (63 patients or 84% of the total). The average age of these patients was 46 years with extremes of 14 years and 69 years... The 75 patients with apparently normal hearts, registering a concave RS-T elevation, were followed for a period of from 1 to 20 years and for an average period of 8 years. So far as I know only two of these patients subsequently developed heart disease. One 38-year-old man developed the typical syndrome of angina pectoris 6 years after his first electrocardiogram had been observed, and for the following 2 years his tracing remained almost identical". The writer considers this RS-T elevation as a special or exaggerated ECG pattern of actual neurosis because all of the patients with this special pattern in their ECG confided very complicated mental conflicts. The one shown in Fig. 14 was recorded on the 1st consultation day. He complained of insomnia, tightness of the chest, dyspnea, a bad dream and malaise. On the 2nd consultation day he confided as follows: He is an adopted son. His foster-mother died after he was adopted. His 2nd foster-mother gave a birth to a boy, and this son is going to get married. There has been a long-continued cold struggle between these 2 brothers of different mothers and different fathers and between his real mother and his 2nd foster-mother about the succession to a property. The other case shown in Fig. 15 is very interesting in that the RS-T elevation seems to have been produced during medical treatment by continued mental conflicts strengthened by doctor's words. On the 1st consultation day he came with a reference of a doctor in a certain Red Cross Hospital, which said the patient had angina pectoris and essential hypertension. He complained of insomnia, palpitation at night, a bad dream and malaise. He was treated by a doctor on that day as an hypertensive. A month later he came for the 2nd time with a reference of another doctor in a certain University Clinic, which said he had cardiac neurosis. But he insisted that there is something wrong with his heart. On the 3rd consultation day at the City Hospital the writer examined the patient for the 1st time. On that day he
offered resistance to the psychoanalytic approach. He repeated that he had no mental conflicts, but his ECG since the 1st consultation day showed a typical pattern of actual neurosis. Three months later he (A) came again exhausted together with his fellow-fisherman (B) who had once been treated by the writer. The ECG recorded on this day showed the typical concave RS-T elevation of Fenchel as shown in Fig. 15c. His complaints were the same as before. On that day, however, he confided everything to the writer. It was revealed that A and B had a bad experience in the sea and lost confidence to live as fishermen. B first became to have a bad headache, ringing in the ears, paresthesia, palpitation at night and malaise and told by a doctor that he might have a cerebral tumor. He was sent to a certain University Clinic and told by a doctor there was no sign of cerebral tumor, and therefore there was no need for further examinations. However, the subjective symptoms still continued. So he consulted a doctor in another University Clinic. There he was recommended to enter the hospital for further examinations. After special examinations he was told by a doctor that there was no cerebral tumor, and so there was nothing to worry about. However, the subjective symptoms became more and more worse. So he consulted a doctor in the department of psychiatry of a certain Prefectural University School of Medicine. There the electroencephalogram was registered, and he was told that there was abnormal waves. B came after all these special examinations to the City

**Fig. 14. RS-T Elevation in a Patient with Complicated Mental Conflicts**

**J.U. 35 Years Old**

a) June 17, 1963, Blood Pressure: 140/90 mmHg

b) August 26, 1963, Blood Pressure: 130/80 mmHg

c) December 19, 1963, Blood Pressure: 140/80 mmHg, BMR: −2%

**Fig. 15. Development of RS-T Elevation in a Patient with Complicated Mental Conflicts**

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Hospital for the 2nd time with a reference of the last doctor who said he should take 0.25 g of aleviatin daily. It was my consultation day and I found that the ECG taken on the 1st consultation day, when he had been recommended to consult a specialist at a University Clinic, showed the Wenckebach period with the typical pattern of actual neurosis. B confided everything to the writer but he did not mention his fellow-fisherman A on that day. Just before A came to the City Hospital for the 1st time his mother was told by a doctor that she had a gastric cancer and was operated, but there was no cancer. B recovered and obtained a new job but A was still suffering from nondescript un easiness and troublesome subjective symptoms. One day B was told that A might commit suicide. So A and B came together and confided as described above. Therefore, the writer considers the concave RST elevation as a special or exaggerated form of the characteristic ECG pattern of actual neurosis. It is interesting to note, however, that all of those 3 patients were engaged in muscular works and looked very manly.

**Summary**

Similarity and difference in ECG between actual neurosis (Aktualneurose) and hyperthyroidism were investigated in 17 patients with hyperthyroidism and 24 patients with actual neurosis from whom concrete contents of stress were drawn out. The ECG in patients with hyperthyroidism without congestive heart failure showed a shortened RR interval, an elevated, normal or depressed concave ST-segment in V4, V5 and V6, a slightly to moderately depressed T wave with a characteristically blunt, round turning point, an increase in the QT ratio, and a complete disappearance of the U wave in V4, V5 and V6. The ECG in patients with actual neurosis showed a normal RR interval, a slightly to moderately elevated concave ST-segment in V5 and V6, a heightened T wave with a characteristically tapering, peaked turning point in V5 and V6, a normal QT ratio and a depressed U wave in V4 and a complete disappearance of the U wave in V5 and V6. The percentage of U wave appearance in hyperthyroidism was 20% in V4 and 0% in V5 and V6. In actual neurosis it was 25% in V4, 2% in V5 and 0% in V6. In controls it was 95% in V4, 85% in V5 and 35% in V6. The QT ratio in V5 averaged 1.01 in controls, 1.04 in actual neurosis and 1.23 in hyperthyroidism. In hyperthyroidism the QT ratio was directly related to the BMR. The T/R ratio in V5 averaged 0.37 in controls, 0.40 in actual neurosis and 0.17 in hyperthyroidism. With a lowering of the BMR, the characteristic ECG pattern of hyperthyroidism changed into that of actual neurosis, and with a continuation of euthyroidism for more than 6 months, a normal U wave appeared in V5 in some cases. The concrete contents of mental conflict could be drawn out from nearly all patients with actual neurosis on the basis of the ECG changes. In some cases a normal U wave was reproduced in V5 after psychoanalysis on the basis of ECG and administration of a tranquilizer for more than 1 month.

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