Isolated U Wave Negativity

By J. H. PALMER, M.D.

Inversion of U as the only abnormal electrocardiographic finding is here shown to be the first change to occur in certain cases of hypertension, coronary artery sclerosis, and other organic heart disease. It is also found in association with certain metabolic and electrolyte changes. Its recognition will enhance the value of the electrocardiogram in clinical diagnosis.

The clinical significance of inverted U waves has received scant attention from cardiologists. Although its association with other electrocardiographic abnormalities has been described,1,2 this has not contributed significantly to diagnosis or prognosis.

Reports of only a very few cases of isolated U wave negativity have appeared in the literature. Nahum and Hoff3 reported two, Papp4 one, and Palmer5 four. In every case the finding was considered abnormal. On the other hand, Katz6 has observed that "little clinical weight would be given to an electrocardiogram in which the only deviation from the normal was in the U wave." The author has shown that U may temporarily become negative during exercise tests for angina pectoris, suggesting that such inversion should be regarded as one of the criteria of acute coronary insufficiency. Valuable confirmation of this is afforded by the later, but apparently independent, observations of Holzmann.6

The physiology of the U wave is imperfectly understood. Hoff and Nahum7 concluded that it forms part of the ventricular complex and is coincident in time with the supernormal phase. Zuckermann and Cabrera8 have suggested that it originates in the interventricular septum and is a result of retardation of repolarization in that structure by the compression brought to bear on it by both ventricles. Zuckermann and Estandía9 later claimed support for this hypothesis by showing that while extrasystoles originating in the ventricular walls usually appear coincidentally with the U wave, those originating in the septum appear after the U wave, that is, at the end of the septal refractory period.

It was felt that while an analysis of clinical records might add little to our knowledge of the causation of the U wave, much might be learned concerning its incidence and clinical significance. Such empirical knowledge is long overdue.

Method

The present communication is based on the findings in approximately 10,000 electrocardiograms personally read by the author in the course of a four-year period during which each tracing was especially observed for negative U waves. Many of the tracings had actually been taken previously and came to notice when being compared with more recent ones. About 7,000 are from a Veterans' hospital where the population is all adult and preponderantly male, 500 are from a children's hospital, and the remainder from a general hospital and from private practice. About two-fifths of the tracings read were normal.

Electrocardiograms were admitted to the series if, apart from U wave negativity, all the leads taken on any one occasion could be regarded as probably within normal range for the patient's age.

U wave negativity that was just perceptible has been accepted, providing it was constant. Alternating current interference will frequently make it difficult or impossible to determine these minor grades; a higher incidence will therefore be found if electrocardiographs are used which minimize or eliminate this interference. We have not resorted to increasing the camera speed, as practiced by Groedel and Miller; they claim by this method a better detection of U waves.

It is frequently found, especially in the right chest leads, and even as far to the left as Cl, that a normally upright T is followed by a negative depression which occupies the period between T
and a positive U. The author has evidence (unpublished data) which suggests that this T-U period is intimately related to the succeeding U wave and may form part of a U complex actually beginning at the end of T. This impression is supported by the observation that diphasic U waves occur and are usually — + in character. They may be seen usually depression and diphasic U waves have not been considered as negative U waves. (See fig. 2.) Identification of a negative U is best made by determining the end of T in other leads and transferring this measurement to the lead in question. In most of the cases in the present series a short isoelectric period between the end of T and the beginning of the negative U could be recognized. Acceleration of the heart rate may cause considerable shortening of the Q-U duration.

It early became apparent that negative U waves in lead aVR were almost as frequently found in clinically normal patients as were upright U waves in other leads. They were assumed to be normal, analogous to the negative T waves seen normally in this lead, and were consequently disregarded. Conversely a positive U in aVR would be considered abnormal; an example of this is shown in figure 1.

**Fig. 1. (Case 31.) Hypertension. Tall thin male with vertical heart showing high degree of clockwise rotation. Negative U waves can be recognized in leads I, aVL, V4, V5, V6, and a positive U wave in aVR.**

at about the C3 position; as the exploring electrode moves further to the left the apex of the U wave negativity concurrently moves further away from QRS (fig. 1).* The matter is still sub judice; in the meantime and for purposes of this paper such T-U

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* A good example of this was discovered in a tracing published by Dressler, Roesler, and Lackner11 to illustrate notching of T waves (their fig. 4).

**Fig. 2. To illustrate depression of T-U junction which may cause confusion with negative U wave. Arrows mark positive U waves.**

**INCIDENCE**

U wave negativity, either isolated or associated with other electrocardiographic abnormalities, was recognized in 165 patients. Ten patients seen early in the investigation (four with isolated U wave negativity) have already been described elsewhere.4 They are included above for statistical purposes, but do not form part of the group to be analyzed below.

In the 500 children's records there was found only one tracing showing negative U waves. This lowered incidence, compared with that in adults, is striking, especially as positive U waves are common in normal children. The
most satisfactory explanation appears to be that the rapid heart rate found normally in infants, usually in sick children, and frequently in healthy children, results in such an approximation of T and P waves that U cannot be recognized satisfactorily.

Fifty-two patients with isolated U wave negativity were found, one for each 200 tracings examined. Some of these patients had two or more examinations, so that the actual percentage of abnormal tracings is considerably higher.

It is a defect in the investigation that unipolar limb leads and multiple chest leads were not taken in every case; had this been done it is possible that some added electrocardiographic abnormalities would have been found, especially in chest leads further to the left in patients with hypertension. Of the 18 patients in the group who had had less than three chest leads in addition to leads I, II, and III, 15 actually had hypertension; all of these had normal-sized hearts (12 proven by x-ray examination), and in three patients subsequent multiple lead tracings proved normal. It is not felt, therefore, that the incidence described above would have been significantly different had 12-lead tracings been made in every case, and moreover such extra leads could well have increased the number of negative U waves found.

In table 1 is recorded the frequency with which negativity occurred in each lead. By far the highest incidence was in chest leads made at the fourth, fifth and sixth precordial positions, in that order. This was reflected to a lesser degree in lead I where negativity did not occur unless at the same time the left chest leads or lead aVL was also involved. No changes were found in C1 and C2. The writer has seen only one case of U wave negativity in the right chest leads,4 and its rarity in this region has been confirmed by Groedel and Miller.10 In only two cases was U negative in lead III, and lead aVF was normal throughout.

**TABLE 1.—Incidence of Isolated U Wave Negativity in Various Leads (48 Cases)**

<table>
<thead>
<tr>
<th></th>
<th>I</th>
<th>II</th>
<th>III</th>
<th>aVL</th>
<th>aVL</th>
<th>aVF</th>
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</thead>
<tbody>
<tr>
<td>11 (48)</td>
<td>1 (48)</td>
<td>4 (48)</td>
<td>—</td>
<td>3</td>
<td>(9)</td>
<td>0</td>
</tr>
<tr>
<td>C1</td>
<td>C2</td>
<td>C3</td>
<td>C4</td>
<td>C5</td>
<td>C6</td>
<td></td>
</tr>
<tr>
<td>0 (12)</td>
<td>0 (28)</td>
<td>1 (7)</td>
<td>44 (46)</td>
<td>17 (20)</td>
<td>5 (15)</td>
<td></td>
</tr>
</tbody>
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Figures in parentheses indicate number of times lead recorded. C indicates chest lead V or F.

of the total number. In four more it was associated with angina pectoris.

In one patient of the hypertension group (case 31) the tracing was made while the patient was in hospital for cystoscopic investigation of his chronic glomerulonephritis and albuminuria. At that time a single normal blood pressure reading was recorded. Six months later the blood pressure was 190/120, and it has since then remained at about this level. The patient was probably hypertensive at the time of the first examination, and has been so classified.

The next largest group is that resulting from coronary sclerosis. It includes nine patients with angina pectoris (four with hypertension, mentioned above), one with coronary occlusion seen in the early stage, and three (cases 7, 21, 34) who, it was assumed on clinical grounds, had asymptomatic coronary sclerosis. In sup-

*At the request of the Editor table 2 is being omitted. It will be furnished upon request.*
port of this diagnosis it is pointed out that one of the three had experienced earlier a paroxysm of auricular fibrillation, another became hemiplegic soon after observation and later developed auricular fibrillation, while the third had an aortic systolic murmur probably indicative of calcific aortic stenosis; all of them were past the age of 75 and were considered senile. The high incidence of extensive coronary sclerosis at necropsy in this age group is well known. Storch and co-workers² have found electrocardiographic changes characteristic of coronary insufficiency in some aged asymptomatic individuals subjected to Master’s standardized exercise tolerance test.

Subsequent reversion of negative U waves to positive (fig. 3) was seen in seven cases of the series, and six of these were in the hypertension and coronary sclerosis groups. In one patient with hypertension (case 27) the tracing was found to be normal as long as five years, and in one with angina pectoris (case 1) three years, after the U wave inversion had been first seen.

The group with valvular disease comprised three cases. One patient had aortic regurgitation with a history of both rheumatic fever and syphilis, another (the only child in the series) had chronic rheumatic mitral disease, and the third had the classic signs of calcific aortic stenosis. The common etiologic agent, if one were sought, would probably be early left ventricular hypertrophy.

An interesting group was found in which the only obvious common factor was elevation of the serum phosphatase level. Two were cases of carcinoma of the prostate (cases 15 and 23, fig. 4), one with bone metastases; in neither of them could any obvious cardiovascular disease be made out. Two patients (cases 19 and 44) had Paget’s disease with high alkaline phosphatase levels; in one of them there was associated hypertension, which of course might itself have affected the U wave. In three of the four cases the serum phosphorus level had been recorded as normal, and in the
only one in which the serum potassium level had been estimated it also was normal. Serum calcium determinations were not made, but it is unusual for them to be abnormal in either of these two diseases. Whether the high phosphatase level is the actual cause of the U wave inversion is a problem which requires further investigation. In Paget's disease another possibility is the load imposed on the heart by the oftentimes greatly increased cardiac output. Such an argument however cannot apply where prostatic cancer is concerned.

The electrocardiographic changes characteristic of hypokalemia are now well known. One of these signs is a prominent positive U wave in the right chest leads. In a patient (case 17, fig. 5) with potassium loss due to carcinoma of the pancreas with small bowel obstruction, a positive U wave of 1 mm., which is large but well within the arbitrary normal limit described by Katz, was seen in V2; there were no RS-T or T wave changes, and the Q-T interval was just within the normal limits. U was negative in leads I and V6. At necropsy the myocardium and coronary vessels were found to be healthy. One seems justified in regarding the U wave changes, both the increased positivity on the right side of the chest and the negativity on the left (they are probably reciprocal), as results of the electrolyte disturbance. Nadler and co-workers found that the U wave present in CR during hypokalemia in diabetic acidosis could be abolished by potassium salts given intravenously, and concluded that U is in some way related to disturbance in electrolyte balance. In any event it would seem that the U wave change is an early one, and that the development of a so-called hypokalemic myocarditis is not essential for its production.

One case of myxedema (case 37) is included. Here the electrocardiogram showed low voltage, but normally directed, T waves; because of its borderline abnormality, it was admitted to the series. Its interest lies in the fact that disappearance of the U wave negativity, present in leads I and V4, was the first change to occur after thyroid treatment was begun. Only later did QRS and T wave voltages increase.

In one case no satisfactory explanation for the U wave negativity could be found. The patient (case 36) had been admitted to hospital for cholecystectomy. No abnormal cardiovascular symptoms or signs were discovered; the blood pressure was normal. Unfortunately it was not possible to trace her subsequently.

**Fig. 5.** (Case 17.) Small bowel obstruction with hypokalemia. U wave negative in leads I and V4. U is unusually high in V2.

**SUMMARY AND CONCLUSIONS**

It has not been the purpose of this communication to determine the mechanism by which U wave negativity is produced, but rather to estimate its frequency and its significance.

Isolated U wave negativity is found in about 1 per cent of routine electrocardiograms from general hospital practice. It is rare in infants and children. Its association with certain diseases, most of which have well-recognized cardiac manifestations, leads to the conclusion on empirical grounds that it is probably always pathologic.

U wave inversion without other electrocardiographic change is seen in patients with hypertension more often than in all other conditions combined. Coronary sclerosis yields the second highest incidence. In both of these diseases and in certain valvular lesions the abnormality is probably related to organic changes in the myocardium. In other conditions in which it was found in the present series, notably Paget's disease, carcinoma of the prostate, hypokalemia, and myxedema, the abnormal process may be biochemical.
The change is an early one, preceding the classic electrocardiographic findings of such chronic diseases as hypertension and coronary sclerosis sometimes by years, and is also reversible.

Recognition of isolated U wave negativity as an early pathologic finding will increase the diagnostic value of the electrocardiogram. Discovery of its association with other diseases than those included in the present series is predicted.

ADDENDUM

Since the above article was prepared for publication 11 further patients have been seen who showed isolated U wave negativity. The diagnoses were as follows: hypertension, six; angina pectoris, one; syphilitic aortic regurgitation, one; calcific aortic stenosis, one; gout, one; pulmonary tuberculosis with duodenal ulcer but without obvious cardiovascular disease, one.

SUMARIO ESPAÑOL

Inversión de la U como el único hallazgo anormal electrocardiográfico es demostrado ser el primer cambio en ocurrir en ciertos casos de hipertensión, esclerosis coronaria y otras enfermedades del corazón orgánicas. También se observa este cambio en asociación con ciertos cambios metabólicos y electrolíticos. Su reconocimiento aumentará la importancia del electrocardiograma en el diagnóstico clínico.

REFERENCES

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