VI. Genesis of the U Wave

By E. Lepeschkin, M.D.

In THE light of our present knowledge, only 3 explanations appear possible for the U wave: first, this wave is caused by a longer duration of the action potential in some section of the ventricles; second, it is caused by afterpotentials following the action potential proper; and third, it is caused by potentials elicited by the stretching of ventricular muscle during the period of rapid filling. In the following we shall examine how each of these hypotheses fits the actually observed behavior of the U wave.

Einthoven[1] originally explained the U wave as due to persistence of electric activity in some section of the ventricle. Zuckermann and Cabrera[2] considered this section to correspond to the interventricular septum, while the recent work of Furbetta, Bufalari, and Santucci[3] indicated that it corresponds to the papillary muscles, since these authors found in hypothermic dogs that the voltage of U was highest in direct leads from points of the ventricular surface near the origin of these muscles. However, if this hypothesis were correct, direct leads from the papillary muscles should show a duration of the T wave or the monophasic action potential corresponding to the Q-U duration in surface leads; this was never observed. Another possibility is that the region with persistent activity corresponds to the specific conducting fibers of Purkinje. Coraboeuf and co-workers[4] found that in intracellular leads from these fibers the duration of the action potential is about 50 per cent longer than in simultaneous intracellular leads from the nonspecific muscle tissue of the papillary muscles. They considered this difference in duration responsible for the normal direction of the T wave; as the duration of the action potential in the Purkinje fibers corresponds to the Q-U rather than to the Q-T duration, these differences could be well held responsible for the U waves. However, the cross-section of the conducting tissue compared with that of the shortcircuiting plain muscle, and accordingly the voltage produced by its activation in surface leads is very small, and certainly cannot account for the tremendous U waves that may appear in hypopotassemia (see below). Furthermore, a U wave can be seen also in the atrium, which has no conducting system, while negative afterpotentials corresponding in time with the U wave appear also in intracellular leads from the ventricular surface, where no Purkinje fibers are present. However, the greatest difficulty in explaining the U wave as due to persistent excitation in some parts of the ventricle is that this explanation would call for the highest voltage of the U wave immediately after the end of the T wave. In other words, the fact that in most cases there is an isoelectric interval between the T and U waves in all leads cannot be explained by this hypothesis.

The second explanation for the U wave is that it is caused by distention potentials of ventricular muscle, originating during the phase of rapid ventricular filling. Distention of ventricular muscle caused a reversible decrease of 1 to 5 per cent in the value of the injury potential,[5-7] which was attributed to a corresponding decrease in the resting polarization of the cell membrane. However, recent experiments of Dudel and Trautwein[8] showed that the true membrane potential, measured by intracellular electrodes is not influenced even by tensions up to 40 times those developed during systolic contraction of the fiber; further stretching causes an irreversible decrease due to injury. The decrease of the injury current by stretching found earlier is attributed to decrease in the diameter of the muscle fibers, with a resultant greater shortcircuiting effect on the injury potential.[8]

From the Division of Experimental Medicine, University of Vermont College of Medicine, and the De-Goesbriand Memorial Hospital, Burlington, Vt.

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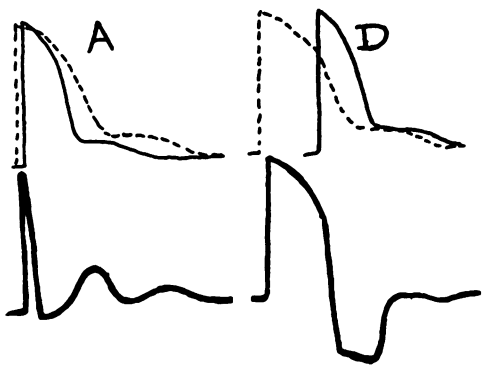

FIG. 1. Schematic construction of the T and U waves as a difference between 2 action potentials with negative afterpotentials. The solid curve represents subepicardial ventricular muscle, which is activated late and has a short action potential. The dotted curve represents subendocardial muscle, which is activated early and has a long action potential; it is an exact copy of the solid curve with a time base extended 1½ times. *A*. Normal conduction. *D*. Delayed conduction, resulting in inversion of T and U.

The best explanation of the U wave is that it corresponds to potential differences produced during the descending limb of a negative afterpotential,* just as the T wave corresponds to similar potential differences produced during the descending limb of the action potential proper. This hypothesis was first made by Nahum and Hoff.[9] Figure 1 illustrates the construction of normal T and U waves based on this assumption; it explains the separation of U from T, as well as the parallelism between the direction of T and U in normal persons and in intraventricular conduction disturbances leading to secondary T wave changes. In this figure, facsimiles have been used of actual intracellular action potentials of the chicken, taken by Fingl, Woodbury, and Hecht[10] since the birds seem to be the only animal species with U waves comparable in size to those of man.[11] In the frog and turtle[12-15] and the dog[8, 15, 16] negative afterpotentials are either absent or do not exceed 3 per cent of the amplitude of the action potential proper; accordingly, these animals show practically no U waves under normal circumstances. Wherever negative afterpotentials have been observed, their position in the cardiac cycle at a given heart rate corresponds perfectly with that of the U wave. Intracellular action potentials have not been registered in the human heart, but in 1 case a negative U wave became transformed into a negative afterpotential when the curve became monophasic due to pressure of the intracardiac electrode.[17]

According to the construction of figure 1 the U wave reflects only the differences in the duration and amplitude of the negative afterpotentials, and not their absolute amplitude; therefore not every change in the U wave would necessarily mean a corresponding change in the afterpotential. However, all factors known to influence the afterpotentials should influence the U wave in the same direction, other things being equal. This is actually the case for all factors studied so far. The negative afterpotential in nerve was attributed[18] to persistence of slight depolarization of the cell membrane after the end of the action potential proper due to the potassium ions that have left the cell during repolarization[19] and are only slowly removed from the cell surface partly by diffusion, partly by active reabsorption into the cell. The descending branch of the action potential of the heart, which corresponds to the T wave of the electrocardiogram, is very probably caused by exit of potassium from the cell, as in the case of nerve.[20, 21] Such an exit during the T wave was actually observed by Wilde and co-workers[22] by means of tracer studies. It is therefore probable that the afterpotentials of heart muscle are also caused by an accumulation of potassium ions that have left the cell during the T wave.[23, 25] If the external potassium is high, less potassium can be expected to leave the cell and more will be reabsorbed during diastole; the negative afterpotentials can therefore be expected to become smaller. Decrease of the extracellular potassium can be expected to have the opposite effect. In agreement with this view, negative afterpotentials of the frog heart,[12] as well as U waves in human beings,[24] decrease regularly

*These afterpotentials were called "negative," since they indicate relative negativity of the cell surface; at the same time they indicate relative positivity of the cell interior, so that they are positive in the intracellular curve of figure 1.

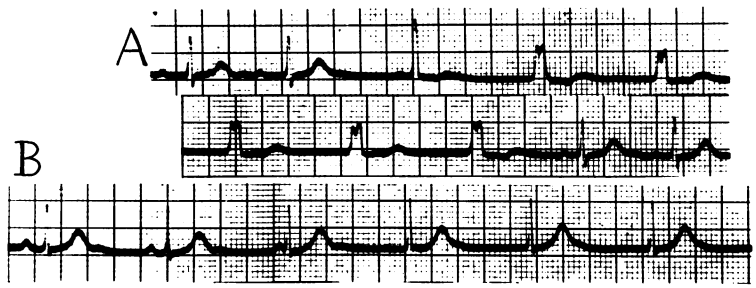

FIG. 2 *A*. Lead I of a young man with tonsillitis, showing ventricular parasystole with fusion beats. The 2 strips are continuous. The beats with wide QRS show inversion of T but little change of U. *B*. Lead II of an apparently healthy young woman, showing partial fusion of T and U during the appearance of an A-V nodal rhythm, without change of heart rate or the configuration of QRS and T.

with increasing external potassium concentration. On the other hand, low serum potassium is characterized by an elevation of the U wave[24, 25] greater than that caused by any other single factor; even dogs and rabbits, which ordinarily show no U waves, develop them when the heart is perfused with solutions low in potassium[26] or when hypopotassemia develops during the course of alkalosis.[27, 28]

Epinephrine causes elevation of both the negative afterpotentials of the frog heart[12] and of the U wave.[29, 30] This effect is probably related to the increased potassium loss from the heart after epinephrine[31, 32]; the elevation of the U wave also can be prevented by administration of potassium.[23] The increase of the negative afterpotentials of the frog heart[12,33] and of the U wave[34] after veratrine can be attributed to decreased velocity of reabsorption of potassium, as in the case of nerve,[18] since it can be prevented by high external potassium[33] which would be expected to increase the rate of reabsorption. The increased amplitude of the negative afterpotential of the frog[12] and of U waves in human beings[35] under the influence of digitalis also can be attributed to inhibition of the diastolic reabsorption of potassium, which is considered responsible for its positive inotropic effect.[36] Calcium has a similar effect on the negative afterpotentials[12] as well as the U wave.[35]

Very significant for the interpretation of the U wave is the finding of Dudel and Trautwein,[8] that stretching causes an increase of the negative afterpotentials of cardiac muscle up to 20 per cent of the height of the action potential. Accordingly, the negative afterpotentials would be expected to be highest in parts of the ventricle subjected to greatest stretch. As a result the U wave tends to show negative polarity in unipolar leads facing these parts and positive polarity in leads facing parts of the ventricle subjected to least stretch and, in addition, tends to have the same direction as the T wave expected from the construction of figure 1. This explanation would fit the observation of Furbetta and co-workers[3] that the U waves are highest on the ventricular surface opposite the insertion of the papillary muscles, for these muscles must bear the entire systolic ventricular pressure that is exerted on the atrioventricular valves. It would also explain the fact that the maximal voltage of U in precordial leads of normal adults is situated slightly to the right of the maximal T wave voltage, and that in children T may be inverted in leads V_1 through V_4 while U is always upright in these leads. It may also account for the fact that in some cases of transient bundle-branch block or extrasystoles, T may become negative while U remains almost unchanged (fig. 2*A*), and that primary changes of T usually do not affect the U wave. That an A-V nodal rhythm may cause the U wave to become taller and begin earlier without any change of heart rate, QRS, or T (fig. 2*B*) can also be explained only by assuming that absence of atrial contraction preceding ventricular systole increases the early diastolic ventricular filling pressure and thus influences the afterpotentials.

Segers[12] found that under conditions of in-

creased intraventricular pressure or in old, anoxic preparations, the negative afterpotentials can be transformed into diphasic and finally into positive afterpotentials; these changes occur at a time when the action potential proper is scarcely modified. A similar mechanism could be held responsible for the primary U wave changes resulting in "isolated inverted U waves" in the presence of upright T waves, which sometimes appear in conditions leading to left ventricular hypertrophy and, less commonly, in myocardial ischemia. Another possibility is that these U waves are caused by an accentuation of negative afterpotentials in the thin ventricular apex, which would be stretched first in beginning dilatation of the ventricle. Only the registration of intracellular or monophasic action potentials in persons with isolated inverted U waves can decide between these possibilities.

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E. LEPESCHKIN

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