Luigi Luciani and the Earliest Graphic Demonstration of Wenckebach Periodicity

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Abstract—Using an isolated frog heart preparation with ligatures around the atria, Luigi Luciani, an Italian physiologist working in 1873 in Carl Ludwig’s famous laboratory in Leipzig, was the first to demonstrate cardiac group beating, which he named periodic rhythm. He attributed this to increased resistance to impulse propagation between the atria and the ventricle. Karel F. Wenckebach, in his 1899 landmark report of group beating in a patient in which he also used pulse tracings, credited Luciani with this discovery. Wenckebach referred to the phenomena as “Luciani periods.” With the advent of electrocardiography in the early 20th century, this form of group beating became known as Wenckebach periodicity and then as Mobitz type I atrioventricular block. We reanalyzed Luciani’s original paper and pulse tracings, and we show that periodic rhythm does indeed meet the criteria of second-degree atrioventricular block as established by Wenckebach. We also reviewed the career of Luciani, who was an important investigator, outstanding teacher and mentor, and distinguished leader of 19th-century physiology. We conclude that Wenckebach still deserves to have his name eponymously attached to this type of atrioventricular block because he was the first to unravel the complicated relationship between atrial and ventricular conduction. (Circulation. 2000;102:2662-2668.)

Key Words: arrhythmia ■ atrioventricular block ■ electrophysiology ■ Luciani ■ Wenckebach

In his classic paper in 1899, Karel Wenckebach described the famous arrhythmia that became known as Wenckebach periodicity and, subsequently, as Mobitz type I atrioventricular (AV) block.1 Wenckebach pointed out that cardiac group beating was an important manifestation of this form of partial AV block, and he referred to the group beating as “Luciani periods.” He credited Luigi Luciani as the first to describe this phenomena in 1873. We studied Luciani’s original article2,3 and review his productive medical career.

The Early Life of Luigi Luciani

Luigi Luciani (Figure 1) was a distinguished Italian physiologist who was an important contributor to the basic understanding of cardiac automaticity, cerebellar function, and the fasting response.4,5 He was born November 23, 1840, in Ascoli Piceno, Italy, and he grew up during a period of political turmoil when Italy was struggling toward unification. His mother came from the noble Italian family Vecchi of Fermo; his maternal uncle was the well-known writer Candide Augusto Vecchi.5 His early schooling was undertaken mostly at home for financial reasons. In 1862, he entered medical school at the University of Bologna, where he was an exceptional student and quickly gained the recognition of his instructors.

I can recall certain events of those first years at the university. My companions nicknamed me the philosopher. The professor of botany complimented me on my final examination, not because I passed the examination, but because I included many particularities that he had not given in his lectures.6

His comparative anatomy teacher wanted Luciani “to remain with him as an assistant for at least 1 year because of my performance in his classes.”6 For health reasons, Luciani transferred to the University of Naples in 1864. There, his teachers encouraged him in a career in anatomy and physiology. Because of a cholera epidemic in Naples the next year, Luciani was forced to return to Bologna, where he completed medical school with distinction in 1868. He stayed as an assistant and then as the full-time Director of Physiology. The studies of the French physiologist Claude Bernard were stimulating to him.

The scientific method of Bernard, the confluence of physiology and pathology that I have studied and practiced for a long period of time were just beginning to be recognized at the University of Naples. I therefore . . . followed this approach with all my energy even though the research means available to me were inadequate.6

Two of his earliest publications, On the Activity of Cardiac Diastole in 1871 and Cardiovascular Phenomenon of Fever and Inflammation in 1872, brought early recognition and the
opportunity to spend 1872 and 1873 working with Carl Ludwig in his physiology laboratory in Leipzig. Looking back at that period, Luciani commented:

Professor Ludwig was not a profound thinker; his temperament was that of a 60-year-old man, always jovial and of simple moods who gathered his young students around him as a shepherd with lost sheep. He was not materialistic . . . But he was principally an outstanding researcher, the leading vivisectionist of Germany, the pioneer of the graphic method in medicine, the discoverer of many facets of hemodynamics and finally, the master of physiology with great numbers of disciples. This trip to Germany signaled a main period of my scientific life because it left in my spirit profound and indelible principles. Out of a sentiment of gratitude and justice that will never be extinguished I recognize Professor Ludwig as my true mentor.

While in Leipzig, Luciani also helped found a society for the purpose of analyzing new work. My stay in Germany was extremely useful to me because of what I had been able to see and hear both from Ludwig and his assistants as well as from my fellow colleagues in the department of research. We founded at Leipzig a “Physiology Society” that met every Saturday evening to discuss the results of our work and present the findings of the most recent and important publications and to establish a true critical scientific approach.

Luciani soon launched his first research project on the frog heart using graphic analysis, as introduced by Ludwig in 1847. Luciani’s observations, On the Periodic Function of the Isolated Frog Heart, were published in 1873 in both Germany and Italy, and they excited great interest and continued research. In this study, Luciani produced group beating in the frog heart. This phenomena became known as “Luciani periods.”

Luigi Luciani’s Experiment

Luciani used a tonographic apparatus for the graphic registration of the ventricular pulse of the frog heart preparation (Figure 2). First, he excised the heart from the frog at the level of the sinus venosus; then, he introduced a cannula into the cavity of the ventricle. A ligature was tied tightly around both atria at different heights above the AV groove. This preparation was connected by tubes to a small mercury manometer, which recorded the oscillations of the internal pressure of the heart.
frog ventricle. A movable glass pin, floating on the mercury column, permitted the ventricular pulse to be recorded on a revolving cylinder. A reservoir of fresh sheep, rabbit, or pig serum maintained the constant filling pressure of the ventricle. A small vessel filled with serum could be raised during the experiment to bathe the outside of the heart, and thus, preserve the preparation.

In Luciani’s study of the course of the action of the frog heart, he observed 3 distinct phases of cardiac activity before the heart was exhausted. The first was the paroxysmal phase (Figure 3). The ventricular pulse rate, by our measurements, was initially rapid at 389 beats/min (bpm), and the ventricular pulse wave amplitude was low. A gradual slowing of the ventricular pulse rate occurred, and 11 s later, the ventricular pulse rate was 38 bpm and the ventricular pulse wave amplitude had increased.

The second phase was “periodic rhythm” or ventricular group beating (Figure 4). The 4 groups of ventricular pulses were composed of 8, 10, 12, and 14 pulses (going from left to right); 3 pauses lasting 5.7, 7.0, and 8.8 s (going from left to right) separated the 4 groups of ventricular pulses. The ventricular pulse rates, by our measurements, were 175, 186, 194, and 205 bpm for groups E, F, G, and H, respectively. Luciani, commenting on the group beating, stated:

This strange effect may continue for 2 or 3 hours, and usually exhibits a regular course. Often the duration both of the groups and of the succeeding pauses declines regularly; at other times it increases in the primary phase, and declines in the next . . . The number of beats in each group has no apparent relation with the duration of the respective pauses . . . The height of the contractions in each group usually forms a descending staircase.² ³

Luciani applied a ligature to different levels of the experimental preparation. When the ligature was applied to the sinus venosus above its opening into the right atrium, no group beating developed. However, “periodic rhythm was an absolute constant phenomenon”² ³ when the ligature was tied at any level of the atria, with groups of shorter duration and pauses of longer duration when the ligature was nearer the AV groove. When the ligature fell on the AV groove, periodic rhythm was absent, or present in only a rudimentary form. Luciani doubted that asphyxia or the toxic action of the serum were the causes of periodic rhythm. Rather, he thought “that the rhythmical activity of the heart is most highly developed in the venae cavae and sinus venosus.”² ³ He reasoned that “the fundamental determining condition of the phenomenon consists in the physiological exclusion of the sinus venosus affected by the ligature” and believed that “the rhythmical impulses . . . encounter resistance,” resulting in pauses during which the impulses “must summate before they can be efficacious,” and that “the resistances . . . determine the periodic rhythm.”² ³

The third phase was the crisis phase (Figure 5). As the heart became exhausted, all periodic group beating ceased. The ventricular rhythm became irregular. We measured the ventricular pulse rate as varying between 21 and 125 bpm. The ventricular pulse wave amplitude remained stable in the dying frog heart. Subsequently, the ventricular pulse slowed and then disappeared.

Luciani described additional observations of ventricular rhythm during his experiments.² “The three phases, paroxysmal, periodic, and crisis, have distinct features but are not always sharply separated . . . and may overlap.” Often “the long pauses are interrupted by isolated contractions,” and “single contractions appear so often in the pauses between the
last groups” of periodic rhythm that he considered them “a forerunner of the crisis phase.” Occasionally, periodic rhythm changed to the crisis phase without interruption by extra contractions during pauses.

Our Analysis of Luciani’s Results

As shown in Figure 4, the paper speed using our measurements is 2.92 mm/s. We calculated the ventricular pulse rate by dividing the number of ventricular pulse waves in each group by the time in seconds from the upstroke of the first ventricular pulse wave after each pause to the upstroke of the last ventricular pulse of each group (ventricular beats/second). This number was multiplied by 60 s/min to get the ventricular pulse rate in beats/minute. The average calculated ventricular rate was 190 bpm (range, 175 to 205 bpm).

To determine the duration of the ventricular pulse wave intervals as measured from the upstroke of each ventricular pulse wave to the upstroke of the next ventricular pulse wave, we enlarged Figure 4 eight times. Using ECG calipers, a magnifying glass, and a ruler, we measured all of the ventricular pulse wave intervals of the enlargements of the 4 groups shown in Figure 4. We then divided the intervals in millimeters by the paper speed in millimeters per second to convert to duration in seconds. These values are summarized in Table 1. To measure the ventricular pulse wave amplitude, we enlarged Figure 4 two times; the height in millimeters of each ventricular pulse wave in the 4 groups was measured at least twice and averaged. These values are summarized in Table 2. Much artifact became evident in all of the enlarged pulse tracings, which made precise measurements uncertain.

Our analysis of Luciani’s recordings in Figure 4 generated two main observations. (1) The interval between the first and second ventricular pulse waves after a pause in each group was greater than the other ventricular pulse wave intervals (Table 1). The interval between the second and third ventricular pulse waves after a pause had the greatest decrease in each group (0.08 to 0.18 s); thereafter, the ventricular pulse wave intervals became shorter, although some intervals lengthened slightly. However, the last ventricular pulse wave interval of groups E, G, and H increased 0.02 to 0.06 s compared with the preceding ventricular pulse wave interval (Table 1). This paradoxical increase of the last interval before the pause was the most common deviation from the classical structure of the Wenckebach phenomenon. (2) After every pause, the first ventricular pulse wave of each group had the greatest amplitude (Figure 4 and Table 2); thereafter, the ventricular pulse wave amplitudes became progressively smaller within each group.

We can infer from the ventricular pulse data presented above that the ligature around the atria and near the AV border of the frog heart decreased AV conduction. The AV pulse interval (equivalent to the PR interval of the ECG) is shortest after each pause and before the first ventricular pulse wave. The interval between the first and second ventricular pulse waves after a pause is the longest because it contains the greatest increment in the AV pulse interval. Although the AV pulse interval continues to increase beat by beat, the increment of AV prolongation decreases progressively; thus, the interventricular pulse intervals tend to become shorter. These are the hallmarks of group beating that Wenckebach more fully analyzed and that became known as Wenckebach periodicity.

The ventricular pulse wave amplitude reflects ventricular stroke volume and is greatest in the first ventricular pulse wave after each pause (Figure 4 and Table 2). The ventricular pulse wave amplitude then declines progressively in each group, suggesting gradual shortening of the ventricular pulse wave intervals and a decrease in ventricular stroke volumes until the next pause (Tables 1 and 2). We noted a marked prolongation of the pauses between each group of ventricular beats: each pause was longer than twice the preceding pause, the interval between the second and third ventricular pulse waves after a pause of each group; 2, the interval between the second and third ventricular pulse waves after a pause of each group; and so forth. Group designations are the same as in Figure 4.

TABLE 1. Variations in the Duration of Sequential Ventricular Pulse Wave Intervals After Pauses

<table>
<thead>
<tr>
<th>Ventricular Pulse Wave Intervals</th>
<th>1</th>
<th>2</th>
<th>3</th>
<th>4</th>
<th>5</th>
<th>6</th>
<th>7</th>
<th>8</th>
<th>9</th>
<th>10</th>
<th>11</th>
<th>12</th>
<th>13</th>
</tr>
</thead>
<tbody>
<tr>
<td>Group E</td>
<td>0.40</td>
<td>0.32</td>
<td>0.28</td>
<td>0.30</td>
<td>0.27</td>
<td>0.30</td>
<td>0.36</td>
<td></td>
<td></td>
<td></td>
<td></td>
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<td>Group F</td>
<td>0.38</td>
<td>0.27</td>
<td>0.26</td>
<td>0.26</td>
<td>0.26</td>
<td>0.21</td>
<td>0.27</td>
<td>0.28</td>
<td>0.27</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Group G</td>
<td>0.44</td>
<td>0.28</td>
<td>0.27</td>
<td>0.27</td>
<td>0.28</td>
<td>0.30</td>
<td>0.27</td>
<td>0.29</td>
<td>0.26</td>
<td>0.30</td>
<td>0.33</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Group H</td>
<td>0.45</td>
<td>0.27</td>
<td>0.29</td>
<td>0.24</td>
<td>0.25</td>
<td>0.27</td>
<td>0.28</td>
<td>0.27</td>
<td>0.25</td>
<td>0.29</td>
<td>0.29</td>
<td>0.28</td>
<td>0.30</td>
</tr>
<tr>
<td>Average</td>
<td>0.42</td>
<td>0.29</td>
<td>0.28</td>
<td>0.27</td>
<td>0.27</td>
<td>0.27</td>
<td>0.30</td>
<td>0.28</td>
<td>0.26</td>
<td>0.30</td>
<td>0.31</td>
<td>0.28</td>
<td>0.30</td>
</tr>
</tbody>
</table>

Values are in seconds. Ventricular pulse wave intervals are derived from Figure 4, which was enlarged 8×. 1 indicates the interval between the first and second ventricular pulse waves after a pause of each group; 2, the interval between the second and third ventricular pulse waves after a pause of each group; and so forth. Group designations are the same as in Figure 4.
ventricular pulse interval. The exact cause of the pauses remains unexplained, but it is compatible with paroxysmal complete AV block followed each time by ventricular group beating with Wenckebach AV periodicity.

In the paroxysmal phase of Luciani’s experiment (Figure 3), the ventricular pulse wave amplitudes (and, by inference, the ventricular stroke volumes) were small when the ventricular rate was rapid. As the ventricular rate slowed, the ventricular pulse wave amplitude (and, by inference, the ventricular stroke volume) increased. By way of contrast during the terminal crisis phase, with exhaustion of the heart, no change occurred in the ventricular pulse wave amplitude or ventricular stroke volume when the ventricular rate changed, suggesting significant ventricular dysfunction (Figure 5).

To illustrate more clearly that the periodic rhythm in Figure 4 represents the first published graphic demonstration of AV block, we arbitrarily assumed that the atrial rate in Luciani’s frog preparation was 33% faster than the ventricular rate. By simple arithmetic and using the ventricular rates in Figure 4 and a conversion factor of 33%, it was possible to calculate the atrial rates. The estimated average atrial rate was 253 bpm (estimated range, 233 to 273 bpm). In Figure 6, the estimated atrial rate was 233 bpm, and the ventricular rate was 175 bpm. To draw the laddergram below Figure 6, a vertical line is arbitrarily drawn on the atrial tier 1 mm before the upstroke of the first ventricular pulse wave of Groups E and F. The estimated atrial pulse interval was 6.0 mm. At intervals of 6.0 mm, vertical lines are drawn on the atrial tier, representing 31 atrial pulses. A vertical line is then drawn on the ventricular tier beneath the upstroke of the 10 ventricular pulses. The atrial and ventricular lines are connected in the usual way.

<table>
<thead>
<tr>
<th>Ventricular Pulse Wave Amplitudes</th>
<th>1</th>
<th>2</th>
<th>3</th>
<th>4</th>
<th>5</th>
<th>6</th>
<th>7</th>
<th>8</th>
<th>9</th>
<th>10</th>
<th>11</th>
<th>12</th>
<th>13</th>
<th>14</th>
</tr>
</thead>
<tbody>
<tr>
<td>Group E</td>
<td>19.0</td>
<td>18.6</td>
<td>18.4</td>
<td>18.0</td>
<td>17.8</td>
<td>17.5</td>
<td>17.0</td>
<td>16.5</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Group F</td>
<td>19.2</td>
<td>18.1</td>
<td>17.8</td>
<td>17.1</td>
<td>16.9</td>
<td>16.6</td>
<td>16.3</td>
<td>16.2</td>
<td>16.1</td>
<td>16.0</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Group G</td>
<td>18.5</td>
<td>17.9</td>
<td>17.3</td>
<td>16.7</td>
<td>16.0</td>
<td>15.7</td>
<td>15.6</td>
<td>15.5</td>
<td>15.4</td>
<td>15.3</td>
<td>15.2</td>
<td>15.0</td>
<td>14.9</td>
<td>14.6</td>
</tr>
<tr>
<td>Group H</td>
<td>18.1</td>
<td>17.0</td>
<td>16.6</td>
<td>16.0</td>
<td>15.9</td>
<td>15.5</td>
<td>15.3</td>
<td>15.3</td>
<td>15.2</td>
<td>15.0</td>
<td>14.9</td>
<td>14.6</td>
<td>14.5</td>
<td>14.4</td>
</tr>
<tr>
<td>Average</td>
<td>18.7</td>
<td>17.9</td>
<td>17.5</td>
<td>17.0</td>
<td>16.7</td>
<td>16.3</td>
<td>16.1</td>
<td>15.9</td>
<td>15.6</td>
<td>15.4</td>
<td>15.1</td>
<td>14.9</td>
<td>14.5</td>
<td>14.4</td>
</tr>
</tbody>
</table>

Pauses

Values are in millimeters. Ventricular pulse wave amplitudes are derived from Figure 4, which was enlarged 2×. 1 indicates the amplitude of the first ventricular pulse wave after a pause of each group; 2, the amplitude of the second ventricular pulse wave after a pause of each group; and so forth. Group designations are the same as in Figure 4.

Figure 6. Ventricular pulse waves of group E (with pause) and of group F as taken from Figure 4, which was enlarged 8×. Our laddergram is drawn beneath waves and illustrates Wenckebach second-degree AV block. Presumed atrial rate is 233 bpm, and the ventricular rate is 175 bpm. A indicates atrial pulse wave; AV, AV pulse wave interval; and V, ventricular pulse wave. Numbers 1 through 10 near top of Figure and beneath laddergram refer to sequential ventricular pulses; numbers 1 through 31 above laddergram refer to sequential atrial pulses. Note Wenckebach AV sequence of first 8 atrial and ventricular pulse waves on laddergram; in addition, eighth atrial pulse wave “jumps over the top” of seventh ventricular pulse wave, indicating that AV pulse wave interval is longer than ventricular pulse wave interval. Next 20 atrial pulses were not conducted; after long pause, Wenckebach AV sequence began again. Paper speed is 23.36 mm/s. Timeline beneath the laddergram has notches at 1-s intervals, and arrow above tracing points in direction of movement of paper. Tracing was lightly retouched for clarity.
The Wenckebach AV sequence of Group E is evident in the first 8 atrial and ventricular pulses shown on the laddergram. After the eighth atrial and ventricular pulse waves of Group E, the next 20 atrial pulses are presumably blocked, resulting in a pause; the same pattern of partial AV block resumes after the long pause. Similar findings are present in the other 3 groups.

**Later Life**

After his research experience under Ludwig’s guidance, Luciani returned to Bologna to teach and to continue his work in experimental physiology. In 1875, he became a professor of pathology at the University of Parma. He then became Chairman of Physiology at the Universities of Sienna (1880 to 1882), Florence (1882 to 1893), and Rome (1893 to 1917). His physiological research interests were broad; they included the automaticity of respiratory centers and Cheyne-Stokes respiration, the function of the spleen, the effects of fever and inflammation, the physiology of edema, the diastolic activity of the heart, the variation of intrathoracic and intra-abdominal pressures, cerebellar function, phonetics, self-intoxication, and the physiology of human fasting. He published 70 articles and books. A treatise on human physiology, *Fisiologia dell’uomo*, was published in Italian, German, English, and Spanish; it became a major textbook of physiology and continued through 5 editions. This was a source of great intellectual satisfaction to him because it stimulated other Italian scientists to publish their own books, which relieved Italian students and physicians from depending on poorly translated foreign texts.

Luciani’s influence and vitality extended beyond his physiological investigations. He was regarded as an outstanding teacher and cardiovascular historian. Like his mentor Carl Ludwig, he produced many future leaders in Italian physiology, pharmacology, and neurology. He also served as a member of the Superior Council of Education, as a senator, and as rector of the University of Rome.

On June 23, 1919, at 78 years of age, Luciani died of a urinary tract infection in Rome. He left behind a reputation that he had enriched science with his brilliant work as a great physiologist and an inspiring investigator. His work can be summed up by his own statement, which was made at a celebration on May 3, 1900, to honor his 25 years as a professor. In this statement, he expressed thanks to his students.

The work to which I dedicated my entire life has been a clean continuous fulfillment of my interest. I have always worked because work itself has given me the greatest pleasure in my life. All my efforts to overcome the serious difficulties that I have encountered in life have not been for me an exercise of virtue but a necessary condition to enjoy the final result. The thought of this psychic pleasure made me insensible to the pain of the effort . . . I do not deserve any credit, I only followed my basic instincts.

**Wenckebach’s Contribution**

Using radial pulse tracings, Wenckebach studied a patient in 1898 who had an unexplained irregular pulse due to cardiac group beating. To help Wenckebach with his investigation of this patient’s puzzling irregular pulse, T.W. Engelmann, his respected mentor, supplied him with pulse tracings recorded in 1893 from a frog atrium and ventricle. By his careful mathematical analysis of his patient’s radial pulse tracings and the tracings from the frog atrium and ventricle, Wenckebach demonstrated cardiac group beating, which he called Luciani periods, and the classic relationships that are known today as Wenckebach periodicity. The signs of Wenckebach periodicity are the following:

1. Small groups of heart beats occur
2. AV conduction is best (shortest) after a pause
3. The greatest increase in AV conduction occurs in the second beat after the pause
4. There is progressive shortening of the ventricular pulse interval after a pause
5. The longest ventricular pulse interval (pause) is less than twice the shortest ventricular pulse interval

**Conclusions**

In 1873, Luigi Luciani was the first to create experimentally and to document graphically group beating. In Figure 4 and Tables 1 and 2, we showed that the group beating and changing ventricular pulse wave intervals and amplitudes in his experiments are consistent with the first 3 specifications of Wenckebach periodicity, as outlined above, and probably with the fourth. Although Luciani did not fully comprehend the atrial and ventricular relationships of this type of partial AV block, he did understand that increased resistance to impulse propagation between the atria and ventricle, produced by a ligature tied at any level of the atria, was the cause of the pauses that he termed periodic rhythm. In 1899, Wenckebach, capitalizing on Luciani’s original observations, was the first to document this in a human and to unravel this complicated relationship. This subsequently became known as Wenckebach AV block and then Mobitz type I AV block. Although the work of Luciani preceded that of Wenckebach by 26 years, we hold that Wenckebach continues to deserve to have his name attached as an eponym to this type of AV block.

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References
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