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Short Articles

ALFRED HENRY GARROD AND THE INDIRECT MEASUREMENT OF THE ISOMETRIC PERIOD OF THE HEART'S CONTRACTION

by

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EXPERIMENTAL PHYSIOLOGY established itself in Britain in the 1870s.[1] With the discipline came a host of new theories and instruments which the physiologists were keen to introduce into medical practice. Instrumentation of clinical medicine did not immediately follow however. One of the first instruments associated with the new physiology was the Marey sphygmograph, which was introduced into Britain in the 1860s and 70s. It was received enthusiastically by a small group of practitioners, principally composed of those sympathetic to experimental physiology. For reasons related to the nature of British clinical practice, and others intrinsic to the instrument itself, it failed to find a warm reception in clinical medicine. The only truly original clinico-pathological investigations performed with the device were those of F.A. Mahomed and Thomas Lauder Brunton.[2]

In the emerging world of physiology the picture was slightly different. The instrument soon found its way into the newly established British physiological texts.[3] In physiological research also it proved to be an extremely valuable investigative aid, notably in the hands of Alfred Henry Garrod.[4] Garrod was born in 1846 and died thirty-three years later of phthisis. His brother Archibald became famous for his work on inborn errors of metabolism. Alfred entered University College in 1862 and studied the natural sciences, notably physiology, and was taught by William Sharpey. In 1868

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[1] See Richard D. French, *Antivivisection and medical science in Victorian society*, Princeton University Press, 1975; and Gerald L. Geison, *Michael Foster and the Cambridge school of physiology*, Princeton University Press, 1978.

[2] Christopher Lawrence, 'Physiological apparatus in the Wellcome Museum: 1. The Marey sphygmograph', *Med. Hist.*, 1978, **22**: 196-200; and 'Physiological apparatus in the Wellcome Museum: II. The Dudgeon sphygmograph and its descendants', ibid., 1979, **23**: 96-101.

[3] Marey's instrument was the one figured in the notorious *Handbook of the physiological laboratory*, London, J. & A. Churchill, 1873, vol 2, Fig. 208, edited by J. Burdon-Sanderson with contributions from the leading British physiologists.

See French, op. cit., note 1 above, pp. 47-50. Similarly the whole of one of Burdon-Sanderson's physiology lectures at University College London was devoted to the Marey sphygmograph. See *Med. Times Gaz.*, 1871, 329-332.

[4] The principal source is Alfred Henry Garrod, *In memoriam. The collected scientific papers*, edited with a biographical memoir of the author by W. A. Forbes, London, R. H. Porter, 1881, pp. ix-xxi. Hereinafter cited as *Collected papers.* See also Casper Rutz, *The Garrods*, Zürich, Zürcher Medizingeschichtliche Abhandlungen, 1970.

he obtained his Licentiateship of the Society of Apothecaries. After a short trip abroad he went in the same year to Cambridge, having been awarded an exhibition for natural science at St. John's College, the first offered in that subject by the college. It was here that he did much of his initial original research and published his first physiological papers. Michael Foster, it might be noted, was appointed praelector in physiology at Trinity College in 1870. Garrod's acquaintance with him may therefore have been slight and he possibly performed his physiological work independently of Foster. Leaving Cambridge, he was appointed Prosector of the Zoological Society of London, taking up the post at the end of 1871. From here on his interest turned to zoological studies, notably comparative anatomy. It was in this area that he published the bulk of his researches. His last physiological paper was published in 1874.[5] In the summer of 1874 he was elected professor of comparative anatomy at King's College London, a post he held almost until his death. In 1875 he was appointed Fullerian Professor of Physiology and in 1876 he was elected a Fellow of the Royal Society. In 1878 he developed a pulmonary haemorrhage and died on 17 October of the following year. Garrod's career is of interest as he was so obviously one of the "new men" of British science. He was clearly influenced by continental methodology in his physiological outlook. He was an indefatigable dissector (he anatomized at least five specimens of rhinoceros). He was a proponent of vivisection, objecting to it only when used purely for educational purposes.[6] He himself had performed probably that most adventurous vivisection to date – after anaesthetizing a giraffe.

Garrod's physiological investigations were centred on body temperature, "the nerve force" and more importantly haemodynamics. In the space of a few years he devised several ingenious experiments using the Marey sphygmograph.[7] Garrod knew of the attempts of Sanderson, Mahomed, and others to use the sphygmograph to measure the arterial tension (i.e. the blood pressure). He was however, sceptical of their conclusions. "The sphygmograph", he noted, "is a bad haemodynamometer at its best." The height of the sphygmographic curve, which was taken as a guide to arterial tension, he regarded as being influenced by too many variables, notably the elasticity of the skin and atmospheric conditions. He concluded that the only constant invariable in the sphygmographic tracing was "the relation borne by the *length* of the different portions of each beat to one another".[8] In consequence Garrod's sphygmographic investigations were directed towards determining the duration of the various parts of the cardiac cycle.

The study of the pressure and time relations of the cardiac cycle had been revolutionized in the early 1860s by the work of Marey and Chauveau.[9] To produce a graphic record of the cycle they devised a cardiac sound or sphygmoscope to record directly the cardiac pressure.[10] The instrument consisted of a hollow metal tube at one

[5] Alfred Henry Garrod, 'On some points connected with the circulation of the blood, arrived at from a study of the sphygmographic trace', *Proc. Roy. Soc.*, 1874, **22:** 140-150. *Collected papers*, pp. 78-90.

[6] *Report of the Royal Commission on the practice of subjecting live animals to experiments for scientific purposes*, London, H.M.S.O., 1876, pp. 106-108.

[7] See Lawrence, 'The Marey sphygmograph', op. cit., note 2 above, Fig. 1.

[8] Alfred Henry Garrod, 'On sphygmography', *J. Anat. Physiol.*, 1872, **6:** 404. *Collected papers*, p. 67.

[9] E. J. Marey, *Physiologie médicale de la circulation du sang*, Paris, Adrien Delahaye, 1863.

[10] See Hebbel E. Hoff and L. A. Geddes, 'A historical perspective on physiological monitoring: Chauveau's projecting kymograph and the projecting physiograph', *Cardiovasc. Res. Bull.*, 1975, **14:** 3-35.

end of which was a wire framework covered with a thin rubber bag. This end was passed down the carotid artery and into the left ventricle of a horse, and the other end was connected to a recording tambour. The rubber bag transmitted the pressure change and by means of the framework was prevented from collapsing. Besides single tracings they made simultaneous records of the changes in the other cardiac chambers, the jugular veins, and the aorta. Though these experiments were attempts to record the intravascular pressures, they also, of course, gave evidence of the time relationships of the cardiac cycle. Comparison of the simultaneous tracings from the left ventricle and the root of the aorta revealed the following fact: "La systole ventriculaire dure donc un certain temps avant d'acquérir le degré d'énergie suffisant pour soulever les valvules sigmoïdes de l'aorte."[11]

In other words, this describes what is now called the isometric period, or the time when the heart's ventricular muscle is unable to shorten because no blood is expelled from the cavities and therefore all the energy developed is expended in raising the intraventricular pressure. In 1863 Chauveau and Marey measured this period in the horse and found it to be about 0.1 sec.[12] The period was frequently remeasured later in the century, and a figure of about 0.02 to 0.04 in the dog was usually taken as the most exact.[13] The period itself was known under a variety of names during the late nineteenth and early twentieth centuries, "the period of rising tension", the "settling" period, the "pre-sphygmic period".[14] It is not in fact a pre-sphygmic period as a wave can be recorded by the optical capsule.[15] The term isometric period was given to it by Wiggers and has been used ever since.[16] Whatever its name, there was apparently no way in which it could be safely measured in man in the nineteenth century. Garrod's achievement was to describe an indirect method of doing so. Garrod's earliest works were simple serial recordings of the radial pulse and an attempt to derive a mathematical law relating arterial systole and the pulse rate (see below).[17] In his next work Garrod developed an investigation formerly used only by Marey.[18] He applied the sphygmograph to the chest wall to record the apex beat.[19] Later, of course, a specific cardiograph was developed for this purpose though the principle was identical. Once again Garrod attempted to derive a mathematical law that described the relations of the cardiac cycle. His next series of experiments were wholly original. He constructed a cardio-sphygmograph which recorded simultaneously the apex beat and the radial pulse; essentially the instrument was no more than two sphygmographs

[11] Marey, op. cit., note 9 above, p. 190.

[12] A. Chauveau and E. J. Marey, 'Appareils et expériences cardiographiques: démonstration nouvelle du mécanisme des mouvements du coeur par l'emploi des instruments enregistreurs à indications continues', *Mém. Acad. Méd.*, 1863, **26**: 268-319.

[13] See for instance E. A. Schäfer, *Textbook of physiology*, Edinburgh, Young J. Pentland, 1900, vol. 11, p. 20.

[14] Ibid., p. 20. R. Burton-Opitz, *Textbook of physiology*, Philadelphia, Saunders, 1920, p. 308. Thomas Lewis, *The mechanism and graphic registration of the heart beat*, 2nd ed., London, Shaw, 1925, p. 25.

[15] Carl J. Wiggers and Harry J. Clough, 'A physiologic investigation into the dynamic action of the heart in functional cardiac disorders', *J. lab. clin. Med.*, 1919, **4**: 624-629.

[16] Ibid., p. 624.

[17] Alfred Henry Garrod, 'On the relative duration of the component parts of the radial sphygmograph in health', *Proc. Roy. Soc.*, 1870, **18**: 351-354. *Collected papers*, pp. 14-17.

[18] Marey, op. cit., note 9 above, p. 68.

[19] Alfred Henry Garrod, 'On cardiograph tracings from the human chest wall', *J. Anat. Physiol.*, 1870, **5**: 17-27. *Collected papers*, pp. 18-26.

tracing on a single paper. The only disadvantage was that the two levers wrote in opposite directions.[20] Garrod's aim was to discover the equations describing the relative lengths of the two cycles.[21] His final innovation was the construction of a double sphygmograph. This device was intended to record simultaneously the radial and posterior tibial pulses.[22]

Using the ordinary radial sphygmograph and making serial observations Garrod derived a mathematical law relating the arterial systolic cycle to the pulse rate.

> The length of the interval between the commencement of the primary and the dicrotic rises in the radial artery is constant for any given pulse-rate, and varies as the cube root of the length of the pulse-beat – being found from the equation $xy=47\sqrt{x}$ where x=the pulse-rate and y=the ratio borne by the above-named part to the whole beat.[23]

Using the sphygmograph as a cardiograph he derived a similar law for the relation of cardiac systole to the whole cycle.

> The length of the interval between the commencement of the ventricular systole at the heart and the closure of the aortic valve does not vary when the pulse-rate is constant, and varies as the square root of the length of the pulse-beat – being found from the equation $xy=20\sqrt{x}$, where x=the pulse-rate, and y=the ratio borne by the above-named part to the whole beat.[24]

It is immediately apparent that the radial systolic cycle or what he called sphygmosystole is shorter than the cardiosystolic phase, a result of course already known from Marey's experiments.

Garrod, besides taking traces from the radial artery, had also taken them from the posterior tibial. He found that the same mathematical law held as at the radial. He confirmed this by using the double sphygmograph: "in which the superposition of the simultaneous posterior tibial trace on that from the radial artery showed that the interval between the commencing primary and dicrotic rises is the same in both."[25] From this observation there followed the corollary: *"the length of this interval is constant throughout the larger arteries, and must be of the same duration at the origin of the aorta that it is in the radial artery at the wrist."*[26] In other words, Garrod had, he believed, the equivalent of a recording of the pulse at the aortic root.

From this corollary followed a valuable theoretical result. Using the cardiosphygmograph Garrod had obtained *simultaneous* recordings of the cardiac and the radial cycle, and from the previous corollary he could compare the different physiological changes going on in the heart with those in the aorta. Garrod concluded that by super-imposing the longer cardiac trace on the shorter radial he would obtain a measure of the isometric period or what he called syspasis. Garrod was, of course, assuming that during the isometric period there is some recordable movement of the heart. This is in fact the case; the base of the ventricle descends and its shape becomes more globular.[27] The two traces can be superimposed because they correspond at the

[20] Alfred Henry Garrod, 'On the construction and use of a simple cardio-sphygmograph', ibid., 1871, **5**: 256-270. *Collected papers*, pp. 27-31.

[21] Alfred Henry Garrod, 'On the mutual relations of the apex cardiograph and the radial sphygmographic trace', *Proc. Roy. Soc.*, 1871, **19**: 318-324. *Collected papers*, pp. 32-41.

[22] Garrod, op. cit., note 5 above.

[23] Ibid., *Collected papers*, p. 79.

[24] Ibid., *Collected papers*, p. 78.

[25] Ibid., *Collected papers*, p. 81.

[26] Ibid., *Collected papers*, p. 81.

[27] Carl J. Wiggers, *Reminiscences and adventures in circulation research*, New York, Grune & Stratton, 1958, p. 239.

end of cardiac systole, i.e. at the closure of the semi-lunar valves.

Garrod gave no details of his experimental procedure, neither the number of trials nor the subjects. Possibly the experiments were performed only once. He tabulated the syspasis for a single series of pulse rates between 36 and 170 beats per minute. He does not state, however, whether their middle range was in a normal subject, whether the higher rates were induced by exercise or were a consequence of disease. Indeed, all the recordings may have been from a single subject.

Garrod found a gradual decrease in the isometric period from 0.06 sec. at a pulse rate of 36 to zero at 170. In the middle range his results are remarkably close to modern figures. At a pulse rate of 64 he found the period to be 0.05 sec. and at 100, 0.022 sec.[28] Garrod had a strong mathematical bent and as a nineteenth-century experimental physiologist a predilection for finding laws governing body functions. In this case he found a strong correlation between the pulse rate and the syspasis. Wiggers in a precise determination of the isometric period using optical and sound recording capsules reported that in heart rates between 56 and 100: "The duration of the isometric period in man is somewhat variable and bears no definite relation either to the heart rate or the duration of systole. The extreme ranges were from 0.025 sec. to 0.08 sec., though the largest number came within the range of 0.04-0.06 sec."[29] In other words, Garrod's range of results was remarkably close to those found by later techniques. However, the precise mathematical correlations he found between particular pulse rates and particular isometric periods do not seem to hold. It seems likely he made these fallacious correlations because of his mathematical bias and his apparently limited number of observations.

It is surprising, actually, how close his results are to more recent estimations considering how inappropriate the sphygmograph is for measuring the time relations at the cardiac apex. Later results were of course obtained using intraventricular recorders. The interest of Garrod's work is twofold. First, it was a remarkable intellectual and technical achievement to obtain, non-invasively, a value for what is at first sight a physiological variable unamenable to such methods. Second, his researches exemplify in some ways the content, status, and relations of British physiology in the late 1860s. Garrod was a lone worker, not working in a physiological school as he would have been on the Continent. His physiological research was performed on man rather than animals, which were not easily come by in England.[30] Finally he was using very simple equipment, the sophisticated laboratory of Germany not existing in London or Cambridge. This was a situation that was to change rapidly over the next ten years.

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[28] Garrod, op. cit., note 5 above. *Collected papers*, p. 82. Garrod's figures were actually given as decimal parts of a minute; I have converted them to seconds.

[29] Wiggers, op. cit., note 15 above, p. 626.

[30] French, op. cit., note 1 above.