Was William Harvey’s commitment to experimentation reflected in his clinical practice?

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Summary
The physician and physiologist Dr William Harvey is known for having discovered that the heart pumps arterial blood round the whole body and receives venous blood from the periphery, which it forwards to the lungs for reoxygenation. Harvey’s discovery was based on anatomical and physiological evidence and experiments using ligatures of varying tensions. As a clinician, however, Harvey does not appear to have appreciated the value of experiments in assessing treatment effects. Although he criticised Galenic views about the clinical value of experience and authority in the absence of accompanying empirical evidence, two handwritten prescriptions that he wrote for his friend and future biographer John Aubrey provide evidence that he conformed with Galenic theory when it came to drug therapy in clinical practice. This was consistent with his senior position in the College of Physicians, whose Pharmacopoeia Londinensis was based on Galenic principles, an appreciation of which was required for entry into the College. Harvey’s prescriptions reflect this and open a window onto 17th-century therapeutic practice and the personal elements on which such practice was sometimes based.

Keywords
William Harvey, John Aubrey, experimental medicine, Galenic theory, humoral theory

Introduction: Harvey’s use of experiments
William Harvey (1578–1657) was a ‘…distinguished physician, the greatest physiologist the world has seen, and the brightest ornament of our College…’. So the College of Physicians (now the Royal College) described Harvey in Munk’s Roll, its collection of biographies of College Fellows.

Harvey is primarily remembered because, using a combination of anatomical observations, blood volume measurements, speculation, and experiments, he demonstrated that blood must circulate around the whole body. His research over the course of a decade culminated in his 68-page book titled Exercitatio Anatomica de Motu Cordis et Sanguinis in Animalibus (An anatomical disquisition on the movement of the heart and blood in animals), usually shortened to De Motu Cordis (1628).

Harvey’s research interests were not restricted to circulatory physiology. In one case he dissected a toad, alleged to be involved in witchcraft practices, to prove that it was simply a toad.¹,² He also saved four innocent women (the so-called ‘Lancashire Witches’) from execution, by refuting witchcraft charges.²,³ In 1620 he even assisted at some archaeological excavations at Stonehenge in Wiltshire (Keynes,⁴ pp. 125–127).

In De generatione animalium, Harvey showed a determination to advance knowledge by experiment, induction and speculation, and he insisted particularly in his writings on the value and importance of experiment (Keynes,⁴ pp. 311, 426). When he donated a library and land to the Royal College of Physicians in 1656, the Trust Deed included ‘an Exhortacion to the ffellowes and members of the said Colledge to search and study out the secret of Nature by way of Experiment’.

What did Harvey mean when he referred to ‘experiment’? In the early 17th century, the word would have implied ‘an action or operation undertaken in order to discover something unknown, to test a hypothesis, or to establish or illustrate some known truth’. Harvey’s exhortation would have been aimed at the first of these.⁵ Chapters 11, 12 and 13 in De Motu Cordis (pp. 48–58) contain descriptions of Harvey’s adoption of an experimental approach in his research, using a ligature as his experimental intervention. Keynes⁴ has summarised these experiments as follows:

[Harvey] described the effects of a tight ligature on a limb, which abolished the blood flow and the pulse altogether beyond the site of application, and of a medium ligature which compressed the vein, but
still allowed blood to traverse the arteries as proved by the presence of a pulse. With the medium ligature the blood could be seen to accumulate in the swollen veins, followed by their emptying towards the heart as soon as the ligature was released... The same thing was seen in the ordinary operation of phlebotomy, where blood flowed more freely from an opening in a vein below the ligature than if it were above. (p. 184)

As Harvey explained in *De Motu Cordis* (Chapter XI, p. 48):

...annotanda sunt experimenta quaedam, ex quibus patet sanguinem in quodcumque membrum per arterias ingredi, & per venas remeare, & arterias vasa esse differentia sanguinem à corde, & venas vasa, & vias esse regrediendi sanguinis ad cor ipsum ['I must describe certain experiments that make it clear that blood enters each part of the body through the arteries and flows out of it through the veins, that the arteries are the vessels that carry blood away from the heart, and that the veins are the vessels and the paths by which the blood returns to that same heart'.]

In a note for his 1627 Lumleian Lecture, Harvey observed:

It is certain from the experiment of the ligature that there is a passage of the blood from the arteries to the veins. And for this reason it is certain that perpetual movement of the blood in a circle is caused by the heart beat. (quoted in Keynes,4 p. 182).

The Latin word that Harvey used to describe his experiment (Figure 1) was ‘experimentum’.

**Harvey’s notes on Galen’s De optima secta ad Thrasybulum**

Harvey’s experimental approach was informed by a critical attitude to supposedly authoritative claims based on the previous experience of others. This can be seen from the Latin marginalia6 in his copy of a 1640 edition of some works of Galen of Pergamon (129–c. 210 AD), collected under the title *Galenii Opuscula hoc Libro comprehensa*, in Latin and Greek, in parallel text. The following examples (Harvey, date unknown) are all taken from *De optima secta ad Thrasybulum* (Aelius Galenus7, pp. 66–143).

Where Galen writes that past experience is not to be taken uncritically (p. 92), Harvey comments ‘it should not be accepted at all, except in diseases and cases in which there is doubt and uncertainty’ ['non admitteretur omnino nisi in morbis et casibus dubiis incertis']; elsewhere Harvey writes, ‘past experience does not support a definitive opinion, although it can be useful in doubtful cases’ ['ex historia non est finale iudicium tamen in re dubia utilis esse potest'].

Where Galen writes that ‘The rational philosopher can pass judgement on the truth or falsity of past events by considering the causes’ (p. 93), Harvey comments: ‘But that is probably not so if the cause is not clear’ ['quia non habet causa vel incertum et obscurum; habeat necne tantum probabile'].

Where Galen writes that ‘The art of medicine is founded on theories derived from and based on outward appearances’ (p. 71), Harvey comments: ‘Not only’ ['non solum']; and elsewhere he writes, ‘theories should be believed only if they can be shown to follow necessarily from the visible signs’ ['nisi demonstratione ex necessariis'].

Where Galen writes that ‘Treatment is simply a matter of applying remedies known to be effective
when certain symptoms are present’ (p. 101), Harvey comments ‘How can this be discovered except by experiment?’ [‘quomodo nisi experimentia’] (Figure 2).

On Galen’s view that we should accept statements by authorities unsupported by evidence (p. 95), Harvey writes,

> When matters are doubtful, I do not trust authorities who disagree with each other, unless they be the best of men. But when things are probable I accept less authoritative views, provided I see no reason not to [‘in re dubia non credidere authoritatibus ubi invicem adversantur nisi probatissimi viri. In re probable cuivis probo viro (si nil me contra movet) debo’].

In another note (p. 102) Harvey suggests that burning curiosity is what makes a physician [‘empyria ergo medicum ratio curiosa facit’].

**Harvey and John Aubrey**

John Aubrey (1626–1697) included his friend William Harvey in *Brief Lives*, his biographical collection of short profiles of 16th- and 17th-century worthy men, as Aubrey called them. Aubrey first met Harvey in 1651, but wrote down his recollections decades after Harvey’s death. Biographers have not always had personal knowledge of their subjects while living, and Aubrey’s writing on Harvey is the most extensive account we have of someone who knew him personally. The publication of *De Motu Cordis* initially did great harm to Harvey’s practice, but by the time of his death he had been vindicated and his discovery recognised as such. Aubrey clearly admired and respected Harvey. He wrote ‘He was very communicative, and willing to instruct any that were modest, and respectful to him’ (Bennett, p. 200). Aubrey noted Harvey’s scientific antecedents by reporting
that Harvey exhorted him to ‘go to the fountainhead, and read Aristotle, Cicero, Avicenna’ (Bennett, p. 201). Aubrey also reported that Harvey did not sympathise with the new Baconian philosophy ‘and did call the neoteriques shitt-breeches’. His disparaging use of the word ‘neoteries’ implies ‘new-fangled’.

Harvey’s clinical practice illustrated with two prescriptions

Two handwritten bills (i.e. prescriptions) from William Harvey to John Aubrey are held in the Bodleian Library at Oxford. They are dated 23 April 1653 and 19 November 1655 (Bennett, p. lxxvi). Both are for a purge to prevent an impostumation, an abscess or a forming abscess. Neither of the prescriptions appears to have been taken to an apothecary, who presumably would have kept them for accounting purposes. We have no context in Aubrey’s personal correspondence as to why he asked Harvey to write the prescriptions (Scurr, p. 107). However, one biographer has noted an event that could have provided a reason for the 1655 prescription, although the event had occurred six months earlier, a riding accident: ‘Then (I thinke) June 14th [1655] I had a fall at Epsam, And brake one of my ribbes and was afraid it might cause an apostumation’.11

Harvey in his lifetime had a reputation for extremely bad handwriting. Aubrey relates

All his Profession would allow him to be an excellent Anatomist, but I never heard of any that admired his Therapeutic way; I knew severall practisers in this town [London] that would not have given 3d for one of his bills [i.e. prescriptions]; and that a man could hardly tell by one of his Bills, what he did aime at’. (Bennett, p. 202)

This could equally refer to the contents of the prescriptions or to their illegibility, perhaps both. Aubrey preserved them as examples of Harvey’s ‘very bad hand’, which he nevertheless claimed ‘(with use) I could pretty well read’.

However, the medical historian Dr Gweneth Whitteridge (1910–1993) deciphered both prescriptions on behalf of Geoffrey Keynes, for his biography of Harvey (Keynes, pp. 439–442). A facsimile of the central section of the original 1653 three-part prescription has been published in ‘A brief visit to William Harvey’ by Michael Hunze. The two prescriptions are shown in Figures 3 and 4 and our analysis of them in Tables 1 and 2.

Interpreting the prescriptions

The verb ‘purge’, which appears in both prescriptions, was used in two senses, both dating from the 14th century. First, to rid the body of harmful (‘naughty’) humours and, second, to cause purgation of the bowel, although it could also mean to cause vomiting.
Of purging medicines Culpeper wrote,

Much jarring hath been among Physicians about Purging Medicines, namely whether they draw the humors to them by a hidden quality, which in plain English is, they know not how; or whether they perform their office by a manifest quality, viz. By heat, dryness, coldness, or moisture.

The major ingredients in these prescriptions, senna, rhubarb, tamarind, hellebore and syrup of roses, all have purgative properties, in the second sense. However, they were also regarded as having the ability to purge humours. Others are carminatives; fennel, coriander and hyssop. Manna was probably added as a sweetener.

Here are the main ingredients:

- Senna: contains laxative anthraquinones, which act by stimulating the bowel.
- Rhubarb: contains laxative anthraquinones.
- Agaric: contains larin.
- Fennel: contains flavonoids, such as quercetin, isoquercetin and kampferol, and phenolic compounds, including gallic acid, p-coumaric acid and chlorogenic acid, some of which may relieve the griping caused by the laxatives.
- Hellebore: Helleborus niger, which contains cardiac glycosides, which in large amounts would be
purgative; there are other plants called hellebore, but they have different Latin names; although in the 1655 prescription Harvey merely writes ‘hellebori’, in the first section of the 1653 prescription he specifies ‘radices Hellebori nigri’, i.e. black hellebore.

- Borage: contains omega-6 fatty acids; the London Pharmacopoeia regarded it as ‘rather laxative than binding’, although that was not its primary use.

- Coriander: probably used here as a flavouring and carminative.

The technical terminology in the prescriptions is explained in Box 1.

**Harvey’s 17th-century therapeutic rationale**

In his experimental approach, Harvey was following in the footsteps of such as Robert Grosseteste,
Roger Bacon, Francis Bacon and Robert Boyle. Why then did he not appear to have the same experimental attitude towards his prescriptions as he did to the physiological problems that he sought to understand? Clues come from other annotations that he made in Galen’s *Opuscula*.

Harvey’s method was based on Galenic theory, following the humoral theory of Hippocrates, which persisted from the time of Galen until the middle of the 19th century. The Greeks distinguished four fluid humours of the body – ἱερός, blood, ψυχικός, phlegm, χολή, [yellow] bile and μέλανω, black bile. According to Galen, in *Περί κρασίουν* (literally *On Blending Fluids*, in Latin *De Temperamentis*), each humour was either warm or cold and wet or dry, and each was associated with a season and one of the four elements, earth, air, fire and water. The mood with which each was also associated was called a temperament: sanguine (optimistic); phlegmatic (stoical); choleric or bilious (irascible); and melancholic (depressive).

Disorders could be treated by giving medicines that affected different humours, thus redressing the supposed imbalance that had caused the disorder. If a disorder was due, for example, to excess blood, it could be treated by bloodletting, or by removal of blister fluid produced by cupping, or by applying agents such as cantharides or mustard plasters (sinapisms), and the use of emetics and cathartics, thus removing ‘naughty humours’.

Furthermore, by the doctrine of signatures, whereby the appearance of a plant denoted its possible uses, white medicines would purge phlegm, black medicines black bile, and yellow medicines choler. In his 1653 edition of the *London Pharmacopoeia* Culpeper wrote, ‘I confess some Ancient Physicians were of this apish Opinion, which in no wise holds true in the general, though in some particulars it may’.

Galen’s method was to combine as many medicines as possible in complex prescriptions, claiming that the body would choose the one it needed. Such prescriptions, known as theriacs or mithridates, were originally developed as antidotes to poisons and venoms, but were subsequently also used as general remedies. Harvey’s prescriptions demonstrate this practice. The supposed Galenic actions of the medicines in Harvey’s prescriptions are shown in Tables 1 and 2.

When Galen suggests that history should be judged by experiment, we might expect Harvey to agree, but when it comes to therapeutic practice he has a different view: ‘many unquestionably excellent treatments cannot be subjected to research in any way’ [‘plurima vero medicamenta eaque optima in historis qualibet ratione probare impossibile’] (p. 93). Techniques to study the efficacy of a treatment, with which we are today familiar, were not available to Harvey. The idea of randomisation, for example, had yet to make its mark. In the *Ortus Medicinae*, posthumously published in 1648, Jan Baptist Van Helmont had proposed a trial of Galenic versus iatrochemical methods, in which lots would be drawn to determine which patients would receive which treatment, but the suggestion was polemical, without evidence that the idea of randomisation, as we understand it, informed it, and the experiment was never performed. George Starkey,
a follower of van Helmont, who had come from New England to London in 1650, later proposed a similar trial, after Harvey's death, but without mentioning the drawing of lots.\textsuperscript{20}

Furthermore, the Galenic view was inimical to an experimental approach, as another remark of Harvey's demonstrates, that 'no-one suffers from a disease in the same way as another, whether it be plague, snake-bite, or the pox' ['sic enim neminem eodem morbi laborare, contendere, non in pestilenta nec ex ictu viperae lue venerea etc'] (p. 88). Each individual requires different treatment, having a different κρασία, a term that Aristotle used to mean the mixing or blending of things that form a compound and also to refer to the temperament of the body (κρασία σώματος) or mind (κρασία χειρονομίας). If no two presentations and no two types of treatment are alike, how can one fairly judge the efficacy of an intervention? Modern methods can deal with this problem, but 17th-century ones could not.

There are more clues in Aubrey's biography of Harvey in \textit{Brief Lives}: 'He did not care for Chymistrey, and was wont to speake against them with an undervalue'.\textsuperscript{11} 'Chymistrey' may have meant the science that we give that name today, a modern-day equivalent perhaps

\begin{itemize}
\item Paracelsus (1493–1541) rejected Galenic humoral theory in favour of a tripartite system reflecting the Trinity and human nature, consisting of soul, spirit and body; he based his therapeutic system on metals and their salts.\textsuperscript{21} Harvey, an ardent Aristotelian,\textsuperscript{22} rejected the Paracelsian view, as he did that of the Helmontians, such as Samuel Hartlib, Noah Biggs, John Webster, George Starkey and George Thomson.\textsuperscript{23,24}
\end{itemize}

Harvey had been a member of the committee of the College of Physicians responsible for preparing the first edition of the \textit{Pharmacopoeia Londinensis} in 1618 and is named there as Medicus Regis juratus, a sworn physician of the King. As a senior physician, Harvey was bound to adhere to Galenic principles. The College promoted them in its pharmacopoeia, despite the Paracelsian views of such as Sir Theodore de Mayerne and Thomas Mouffet.\textsuperscript{25} In his 1653 edition of the pharmacopoeia,\textsuperscript{12} contemporaneous with Harvey's prescriptions for Aubrey, Nicholas Culpeper gave an extended account of Galenic theory, dividing different medicines into 24 types, starting with emollient medicines and hardening medicines and ending with purging medicines. And anyone seeking entry to the College was required to demonstrate a knowledge of Galenic texts and principles, as affirmed in the College's revised statutes of 1647.\textsuperscript{26}

Aubrey also mentions Harvey's attitude to Francis Bacon:

\begin{quote}
[Harvey] had been physitian to the Lord Chancellor Bacon, whom he esteemed much for his witt and style, but would not allow him to be a great philosopher. 'He writes philosophy like a Lord Chancellor' said he to me, speaking in derision; 'I have cured him'.
\end{quote}

Bacon, although an affirmed experimentalist (Donaldson 2013),\textsuperscript{15} was also a supporter of the Paracelsian view.

\section*{Conclusion}
The two prescriptions we have illustrated here are Galenic purges to prevent or treat an impostumation—an abscess. The purges were intended to restore balance within the humours, previously set out of balance by the evolving abscess. It is highly unlikely that they would have prevented or ameliorated an infection of that sort, but they would certainly have caused purgation, in the sense of an increased bowel movement. It is of interest that Harvey's experimental approach to physiology, exemplified by his seminal discovery of the circulation, had no discernible effect on his therapeutic practice, or indeed the perceived, or then understood, nature of the prescriptions he wrote. The prescriptions reflect a very different understanding from our own, although in his time they would have been regarded as rational, causal, and predictive.

Few of William Harvey's prescriptions written in his own hand survive, but there are two others: 'Dr Harvey prescription March 6' and 'Dr Harvey June 28, 1647'.\textsuperscript{27} The phrase 'my honoured friend' on the extant prescriptions is seen only in the Aubrey prescriptions, indicating the depth of friendship between the two men. The 1655 prescription is dated 18 months before Harvey's death on 3 June 1657 and was issued at a time when he practised little, or rarely; indeed he had gone into near retirement by then. As Aubrey wrote, 'His practice was not very great towards his later end, he declined it, unless to a speciall friend...'.\textsuperscript{8} Aubrey, in his \textit{Brief Lives}, does not relate that he was ever personally treated by Harvey. Perhaps the inscription 'my honoured friend' implies that the prescriptions were never intended to be used, but were given as keepsakes, nothing more than to obtain Harvey's signature in the full manner in which it would have been professionally used. A modern-day equivalent perhaps would be obtaining the signature of Her Majesty Queen Elizabeth II through a pardon.
The other element here is a personal one. We are not discussing an anonymous prescription for an anonymous biographer. Aubrey, one of the supreme 17th-century voices, deliberately, carefully and safely kept Harvey’s prescription. He clearly regarded Harvey highly, not only as a physician through his work and actions, but more importantly as a friend. An analogous contemporary example is that of poet laureate Andrew Motion, writing of his longstanding poet friend Philip Larkin.

But Aubrey’s biography of Harvey relates a final poignancy. In a deep mark of loyalty to his friend, Aubrey himself was one of the pallbearers at Harvey’s funeral and helped to carry Harvey’s coffin to its final resting place. Aubrey does not mention in Brief Lives ever having done this for anyone else.

So in these sheets of paper we have two prescriptions, two names, a method of therapeutic practice unaffected by a major experimental revolution in physiological understanding, a friendship and an act of deep remembrance.

The prescriptions, which illustrate the two men’s friendship, show that Harvey was bound by the therapeutic conventions of his day, as dictated by established Galenic principles, with which they are completely consistent, rather than by the application of experiment or the results of experiments done by others. Harvey’s writings suggest that this may have been because, great experimentalist though he was, he had not conceptualised experimental tools with which to put therapies to the test.

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References


22. Pasipoularides A. Greek underpinnings to his methodology in unraveling De Motu Cordis and what Harvey has to teach us still today. *Int J Cardiol* 2013; 168: 3173–3182.


