

Sailors, scurvy and science

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INTRODUCTION

The controlled clinical trial means merely introducing the ordinary, accepted criteria of a good scientific experiment.

Sir George Pickering, 1960¹

The history of medicine abounds with remedies that were long and widely used before falling into disrepute and vanishing. A designed test might have greatly hastened their fall from favour and have thereby encouraged the search for something better¹.

To claim that today's medicine is free from empiricism would be rash indeed, but the stringent requirements for licensing of new drugs and the rise of evidence-based medicine do ensure that therapeutic measures are judged increasingly on the scientific evidence and decreasingly on the force of personality, standing in the profession, or fervour of the protagonists. The best tool for providing this evidence is usually the prospective randomized control trial².

Looking at the history of drug evaluation, Green³ subdivided the agents into three groups—those used as a result of observation and empiricism; those used on the basis of authority; and those used on the basis of experiment.

Little can be said in favour of authority alone as a criterion of value in therapeutics. The undue longevity of many useless and even harmful drugs or modes of therapy can be laid at the door of authority. A good example of this type of approach was the use of copious bleeding and purging by Benjamin Rush during the yellow fever epidemic in Philadelphia in 1793⁴. Rush, a signer of the Declaration of Independence, was one of the most famous men in America, and he 'knew' that bleeding and purging was beneficial for his patients. Rush's approach to treatment was full of misguided fervour, but at the time he was essentially unchallenged because of his distinguished position.

While treatment based on scientific experiment in the form of randomized trials has nowadays come to dominate our approach to disease, this has not always been the case and it is instructive to review the beginnings of the development that led ultimately to the modern controlled clinical trial.

EARLY CLINICAL STUDIES

In the history of therapeutic experiments, there is little evidence of any deliberate attempt to test the value of treatment before the eighteenth century⁵. There were, for example, the experiments on smallpox inoculation in the eighteenth century carried out on the orders of Queen Caroline on prisoners at Newgate prison, and on 'charity children', before she would allow her own royal children to be inoculated. Luckily, these experiments were successful in that the subjects were protected without any serious ill effects. Such experiments are interesting early examples of prophylactic trials in 'volunteers', who in those days were rewarded for their services either with their lives if they were condemned criminals or, in the case of children, by money or other bribes. Later in the eighteenth century, there were Edward Jenner's beautifully reasoned and critically observed trials of vaccination with cowpox. William Withering's monumental 10-year study of the foxglove as a remedy for cardiac dropsy was notable for the use of 'unselected cases' and for his observations of the effect on the pulse rhythm and urinary output as yardsticks to check the validity of subjective improvement.

The first authenticated example of a therapeutic experiment with controls appears to have been James Lind's trial in 1747 of the value of oranges and lemons in treating scurvy in sailors, for which he can properly be considered the father of the controlled clinical trial^{5,7}. Lind

... undertook the study of an important and devastating disease, considered it from every aspect, and propounded measures for its prevention and cure which, on their application, grew so successful that the disease ceased to have any practical importance⁷.

It is given to very few members of the medical profession to achieve so much and the fact that at the time of his landmark experiments he was an obscure naval surgeon only makes the story more dramatic. Unlike most of his contemporaries, Lind in effect admitted that he did not know how to treat scurvy, and therefore conducted an experiment.

CONDITIONS IN THE ROYAL NAVY

Some idea of what conditions were like in the Navy when Lind joined as a surgeon's mate is given by Tobias Smollett in his novel *Roderick Random*, published originally in 1748⁸. Like Lind, Smollett had been a Scottish medical student, graduating from Glasgow in 1739—the same year that Lind

joined the Royal Navy. Again like Lind, he came south to make his fortune and circumstances compelled him to seek employment as a surgeon's mate. If Lind's examination for the Navy was anything like that of Smollett's hero, Roderick Random, the examination was farcical. In the novel, Random was summoned by a beadle to appear before a table of grim-faced examiners, who asked his qualifications and informed him that '... it was a shame and a scandal to send such raw boys into the world as surgeons'. We need not take too literally the question that was posed to Random: 'If during an engagement at sea, a man should be brought to you with his head shot off, how would you behave?', but there can be little doubt that such examinations, which lasted a quarter of an hour and ended with a demand for a five shilling fee, were perfunctory in the extreme. When Random arrived on board his ship, he was shown down to the surgeon's mess, which consisted of a space about six feet square, surrounded with medicine chests and a canvas screen. When he sees the sick berth he exclaims:

I was much less surprised that people should die on board, than that any sick person should recover. Here I saw about fifty miserable distempered wretches, suspended in rows, so huddled one upon another, that not more than a fourteen inch space was allotted for each with his bed and bedding; and deprived of the light of day as well of fresh air; breathing nothing but a noisome atmosphere of the morbid steams exhaling from their own excrements and diseased bodies, devoured with vermin hatched in the filth that surrounded them, and destitute of every convenience necessary for people in that helpless condition⁸.

Although in his novel Smollett undoubtedly exaggerated his early experiences as a ship's surgeon, there is little reason to think that the conditions that Lind encountered at sea were much better.

Today, it is difficult to imagine how sailors lived in the eighteenth century, and indeed well into the nineteenth century. David Howarth⁹ gives a vivid description of conditions even 50 years after the time that Lind was making his observations.

The most evocative glimpse ... was given by a boy named Bernard Coleridge. His ship was blockading Brest, and he was 11 years old, and he wrote to his father and mother: 'Indeed we live on beef which has been ten or eleven years in corn and on biscuit which quite makes your throat cold in eating it owing to the maggots which are very cold when you eat them, like calves-foot jelly or blomonge being very fat indeed. ... We drink water of the colour of bark of a pear-tree with plenty of little maggots and weavils in it and wine which is exactly like bullock's blood and sawdust mixed together.

Howarth continued:

Not many artists who painted [sailing ships] had also lived in them. People who had knew only too well that they were damp, insanitary

and overcrowded, with no provision whatever, except in the officers' cabins, for any physical comfort. Every description of them ought to evoke a smell—of tar, bilge water, sodden timber, old salt meat, rum, gunpowder and closely packed human bodies ... Nelson's ships could stay at sea as long as the strength of their officers and men would let them: all they needed, once in three months or so, was food and water from supply ships or from boats in the outer roadstead of a port ...

Nelson, blockading Napoleonic France, was two years without setting foot off the decks of his ship, HMS *Victory*, and Collingwood had once been at sea for 22 months without ever dropping anchor⁹. It is thus hardly surprising that the sailors in such ships came down in droves with deficiency diseases. Perhaps the wonder of it is that any of them managed to survive their long voyages.

SCURVY AMONG SAILORS

Scurvy was a very prevalent disease in Lind's day, and sailors were particularly susceptible. The doctrines and therapeutics of the great Boerhaave of Leiden completely dominated medical teaching in Europe at that time, especially in Edinburgh. Comparing Boerhaave's account of scurvy, with its emphasis on the use of mercurial compounds, is to realize what an immense stride Lind had made on ideas then prevalent in academic medicine. The earliest medical writers on scurvy were Dutch, and in the sixteenth century its practical aspects—diagnosis, causes, prevention and cure—were well recognized and understood by both laity and doctors. Not only was the cure of scurvy by fresh vegetables a matter of common knowledge, but the value of oranges and lemons was also known to Dutch sailors who brought cargoes of these fruits from Spain. For some reason, all this knowledge seems to have been forgotten, and by the early eighteenth century there was much ignorance about the disease. The general misconceptions regarding the malady had a deplorable and far reaching effect on its prevention and treatment. This may have been due to the labelling of many conditions as scurvy, traditional antiscorbutic herbs being found ineffectual against such an array of heterogeneous diseases. Accordingly, during the late seventeenth and early eighteenth centuries, there was much confusion about what scurvy was and how it was best treated⁵.

Many examples could be quoted of the havoc that scurvy caused among sailors in their voyages around the world, and there are several vivid descriptions of the terrible effects of this disease. One example will suffice, taken from the account of Lord Anson's voyage around the world from 1741 to 1744. Anson was commander-in-chief of a squadron of ships sent on an expedition to the South Seas. He sailed from Portsmouth with almost 2000 men in six fighting ships and two supply ships. Having circled the world, they returned to port after four years at sea. But of the 2000 men

that had left Portsmouth, only 200 returned home, most of the rest having died of scurvy⁵. This famous voyage of Lord Anson, which was only one of many such voyages with disastrous consequences, was partly instrumental in stimulating Lind's investigations of scurvy. Lind conducted his experiments just three years after Anson returned from his voyage around the world.

JAMES LIND

Lind was born in Edinburgh on 4 October 1716 and at the age of 15 he began his medical studies. This was in 1731, and he seems to have received his whole professional education in Edinburgh⁵. As was typical of his time, he received the bulk of his professional training from his work and experience as an apprentice. Like many Scots before and since, after finishing his education Lind moved south to seek employment, and in 1739, at the age of 23, he entered the medical service of the Royal Navy. He had no degree or qualifications except for his apprentice indentures, and so he joined the Navy in the humble capacity of surgeon's mate. During his 10 years at sea, Lind saw service in the English Channel and sailed to the Mediterranean and the West Indies. After leaving the Navy in 1748, he graduated MD at the University of Edinburgh, where surprisingly his doctoral thesis had nothing to do with scurvy. It was not until some years later (1753) that the first edition of his classic text, *A Treatise of the Scurvy*, was published in Edinburgh⁶.

LIND'S CLINICAL TRIAL

In his *Treatise of the Scurvy*, Lind describes scurvy from all aspects, including a critical history of the different accounts of the disease, the true causes of the disease from observations made upon the condition on land and sea, the diagnostics or signs, and the prophylaxis or means of preventing this disease, especially at sea⁶. In the fourth chapter of part two, he gives an account of his experiments at sea in May and June of 1747. He was at that time serving as the surgeon on board HMS *Salisbury*, a fourth rate frigate with 60 guns, and they were on a cruise in the English Channel. In chapter two of his book, entitled *The Diagnostics or Signs*, Lind gives an account of the disease as he saw the condition in sailors. The clinical picture that he describes is worth quoting, as few are familiar with it today:

The first indication of the approach of this disease is generally a change of colour in the face, from the natural and usual look, to a pale and bloated complexion; with a listlessness to action, or an aversion to any sort of exercise. Their former aversion to motion degenerates soon into an universal lassitude. . . . Their gums soon after become itchy, swell, and are apt to bleed upon the gentlest friction. Their breath is then offensive; and looking into their mouth, the gums appear of an unusual livid redness, and soft and spongy, and become afterwards extremely putrid and fungous; the pathognomonic sign of

the disease. They are subject not only to a bleeding from the gums, but prone to fall into haemorrhages in other parts of the body. Their skin . . . is found covered with several reddish, bluish or rather black and livid spots, equal with the surface of the skin, resembling an extravasation under it, as were from a bruise. These spots are of different sizes, from the bigness of a lentil to a handsbreadth and larger. Many have a swelling of their legs; . . . it gradually advances up the leg and the whole member becomes oedematous . . . whatever former ailment the patients has had . . . or whatever present disorder he labours under, upon being afflicted with this distemper, his former and old complaints are renewed, and his present malady, whatever it be, are rendered worse.

Lind's account of the disease continues:

In the second stage of this disease, they most commonly lose the use of their limbs; having a contraction of the flexor tendons in the hand with a swelling and pain in the joint of the knee. They are apt, upon being moved, or exposed to the fresh air, suddenly to expire. Scorbutic people are at all time, but more especially in this stage, subject to profuse haemorrhages from different parts of the body; as from the nose, gums, intestine, lungs, etc. and from their ulcers, which generally bleed very plentifully. The gums are for the most part excessively fungous, with an intolerable degree of stench, putrefaction, and pain sometimes deeply ulcerated, with a gangrenous aspect. The teeth most commonly become quite loose and often fall out. . . . Towards the close of this malady, the breast is most commonly affected with a violent and uneasy straitness and oppression, and an extreme dyspnoea; accompanied sometimes with a pain under the sternum, but more frequently in either of the sides: while others, without any complaint of pain, have their respiration become quickly contracted and laborious, ending in sudden, and often unexpected death.

Lind then gives a graphic but succinct description of the experiment that he carried out on his patients.

On the 20th of May, 1747, I took twelve patients in the scurvy, on board the *Salisbury* at sea. Their cases were as similar as I could have them. They all in general had putrid gums, the spots and lassitude, with weakness of their knees. They lay together in one place, being a proper apartment for the sick in the forehold; and had one diet common to all. Two of these were ordered each a quart of cyder a-day. Two others took twenty-five gutts of elixir of vitriol three times a-day, upon an empty stomach. Two others took two spoonfuls of vinegar three times a-day, upon an empty stomach; having their gruels and their other food well acidulated with it, as also the gargle for their mouth. Two of the worst patients, with the tendons in the ham rigid, (a symptom none of the rest had), were put under a course of sea-water. Of this they drank half a pint every day, and sometimes more or less as it operated, by way of gentle physic. Two others had each two oranges and one lemon given them every day. These they ate with greediness, at different times upon an empty stomach. They continued but six days under this course, having the quantity that could be spared. The two remaining patients, took the bigness of a nutmeg three times a-day, of an electuary recommended by a hospital surgeon. The consequence was, that the most sudden and visible good effects were perceived from the use of oranges and lemons; one of those who had taken them, being at the end of six days fit for duty. The spots were not indeed at that time quite off his body, nor his gums sound; but without any other medicine, than a gargarism of

elixir vitriol, he became quite healthy before we came into Plymouth, which was on the 16th of June. The other was the best recovered of any in his condition; and being now deemed pretty well, was appointed nurse to the rest of the sick.

Although Lind probably did not randomly allocate the patients in his study into the six groups he described (and indeed it was to be another 200 years before a strictly controlled trial was carried out), he clearly recognized the need to compare different treatments, which is an essential point of any clinical trial. Lind had the foresight to perceive that the only way to evaluate a remedy was to compare it *simultaneously* with other accepted treatments in comparable patients. The beauty of his experiment was that it was a concurrent study under identical conditions, comparing various types of therapy commonly used for the treatment of scurvy at that time. All the patients were housed in the same space, and he was therefore able to refute suggestions that bad air or crowded conditions were primarily responsible for scurvy aboard ships at sea. Lind declared: 'I shall propose nothing merely dictated from therapy; but shall confirm all by experience and facts, the surest and most unerring guides'. His therapeutic recommendations were based not only on his general clinical experience, but on exact comparative observations carried out on patients in hospital given remedies, a method that was a novelty at the time. It is of interest that Lind regarded scurvy as principally and mainly due to the prevailing damp and general discomfort aboard the ship among common seamen, with close confinement, depression of spirits and antecedent illness, 'an additional and extremely powerful cause being the want of fresh vegetable and greens'. Lind recognized clearly that the disease in seamen was far more than just the lack of ascorbic acid.

SUBSEQUENT CAREER

In 1758, Lind was appointed physician to the Royal Naval Hospital at Haslar, Portsmouth, whereupon he resigned as Treasurer of the Royal College of Physicians in Edinburgh. His salary was £200 a year, but he was also allowed to engage in private practice. He worked for 25 years as the medical chief of Haslar Hospital, which was the main naval hospital in England and indeed at the time was one of the largest hospitals in Europe. At Haslar, Lind acquired an enormous clinical experience of scurvy. In his first two years of office he stated that, of the 5743 admissions, one-fifth were cases of scurvy. During the seven years of war with France and Spain, he usually had 300 to 400 cases of scurvy under his daily charge in the hospital, and even as many as 1000 cases at one time. Lind's personality and abilities seem to have attracted little attention during his lifetime, except from a small group of his professional naval colleagues who admired him and looked up to him as an authority on all

matters connected with the diseases of seamen. Even though Lind became the medical head of Haslar, he received no honours or public recognition of any kind from the Admiralty or indeed from any of the learned bodies in England and Scotland⁵.

The record of his work attests to the fact that Lind possessed an original and independent mind. One of his disciples, Thomas Trotter, wrote that 'the leading trait of his professional character has marked him a man of observation'. It is clear that he drew his conclusions only after carefully conducted comparative trials of numerous different remedies. Little is known of his personal characteristics, but he was reported to be modest and unassuming and imbued with the true spirit of scientific enquiry. His famous experiment was conducted in 1747, yet he did not publish the results until 1753. While few today would wait 6 years before publishing the results of their experiments, the delay is perhaps a reflection of the more leisurely pace of life in the eighteenth century. Two quotes from his writings will suffice to convey the quality of his intellect:

Of theory in physic, the same may perhaps be said as has been observed by some of zeal in religion, that it is indeed absolutely necessary; yet by carrying it too far it may be doubted whether it has done more good than hurt in the world.

Another of his comments is perhaps even more revealing: 'The Province has been mine to deliver the Precepts; the power is in others to execute'. James Lind clearly recognized that his position as a surgeon in the Royal Navy in the mid-eighteenth century was such that he had little power to see that his recommendations were carried out.

Lind died at Gosport on 17 July 1794, 41 years after his *Treatise of the Scurvy* was published, and just as his recommendations were being put into effect in the Royal Navy. Incredible though it may now seem, his advice regarding the prevention and treatment of scurvy was ignored until 1794, when Sir Gilbert Blane arranged that a small squadron of ships destined for the East Indies should be furnished with an adequate supply of lemon juice. However, by the time of Lind's death most ships had a supply of lemon juice, and scurvy was becoming a thing of the past, at least in the Royal Navy. For example, in 1803 Trotter commented that 'a case of scurvy requiring to be admitted to the hospital has not come under my observation since 1795'⁵. It seems likely that scurvy was largely abolished in the Royal Navy around 1800, oddly enough without any general order for ships to issue antiscorbutics¹⁰. It is a sad commentary on the naval bureaucracy of the day that there was a quite inordinate delay in instituting a lemon juice ration in ships. The truth seems to be that medical schools and writers were

obsessed with their theories and, when officially consulted, as they often were, they gave very poor advice. Even naval medical officers, who knew about the ravages of scurvy at first hand, failed to grasp the full bearing of Lind's teachings.

Lind's *Treatise of the Scurvy* has been described as follows:

Through its presentation of the subject, with its devastating criticism of superstition and muddled thinking, its insistence on careful observation and controlled experiment, its rigid reliance on facts and its logical interpretation of them, it became one of the great medical classics of all time⁷.

The harsh conditions of life in the Royal Navy in the 1740s were certainly not conducive to medical experiments, yet Lind was able to make crucial observations that led eventually to the eradication of a serious and prevalent disease. Perhaps an even more important legacy was that he established a scientific basis for investigating remedies.

Lind can be considered a forerunner of the modern clinical investigator, with faith in the validity of his own observations and the logic of his deductions from them—even though these seldom conformed to the established ideas of his time. The essential feature of Lind's genius was the power to observe and record the natural history of disease with an open mind, untrammelled by the preconceived notions of previous writers. This allowed him to accept the results of his controlled clinical trial, and to recognize that

he had found an effective remedy for scurvy. Only today are we realizing fully the importance of the scientific approach to treatment that was pioneered by James Lind on board the *Salisbury* at sea. The manner in which he demonstrated how scurvy could be cured was a triumph of the scientific method, and it is for this that he should also be remembered.

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