Knowledge Transfer and the Complex Story of Scurvy

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Looking at historical examples through the lens of complexity can provide a fresh perspective on many hitherto standard examples. In this paper I would like to explore the story of scurvy which has been widely presented as an example of difficulties in the application of scientific results and to recognize the complex nature of this process. Apart from being a good sea yarn with lots of twists and turns, the story can contribute important insights to our understanding of the complex nature of the interactions between research and practice and cast some doubt on the more formulaic accounts of the processes that underlie such emerging fields of knowledge translation and knowledge brokerage.

In 1747 James Lind was a surgeon on the HMS Salisbury. After a second outbreak of scurvy on the ship he conducted his now-famous experiment, which is widely recognized and celebrated as a very early clinical trial. He selected twelve sailors suffering from scurvy and divided them into six groups of two. All were given a similar diet of "water gruel sweetened with sugar in the morning; fresh mutton broth often times for dinner, at other times boiled biscuit with sugar etc and for supper barley and raisins, rice and currants sago and wine or the like"(Lind, 1753:145). He then treated them using the following treatments (here quoted in full but reformatted with modern bullet points to differentiate the six groups):

- Two of these were ordered each a quart of [hard apple] cider a-day.
- Two others took twenty-five “gutts” [drops] of *elixir vitriol* [dilute sulfuric acid], three times a-day, upon an empty stomach; using a gargle strongly acidulated with it for their mouths.
- Two others took two spoonfuls of vinegar three times a-day upon an empty stomach; haveing [sic] 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 of 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 [laxative].

- 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 consumed the quantity that could be spared.
- The two remaining patients, took the bigness of a nutmeg three times a-day, of an "electuary" [medicinal paste] recommended by an hospital surgeon, made of garlic, mustard seed, *rad. Raphan*[dried radish root], balsam of Peru [resin from the balsam tree] and gum myrrh; using for common drink barley-water well acidulated with tamarinds; by a decoction of which, with the addition of *cremor tartar* [potassium hydrogen tartrate], they were gently purged three or four times during the course. (Lind, 1753:145-146)

This experiment, often celebrated as the first modern clinical trial, offered clear results. The two sailors given oranges and lemons, even though it was for only six days, were much improved; one of them was "appointed nurse to the rest of the sick"(Lind, 1753:146). The results are completely apparent, the conclusion overwhelming. Lind published his *Treatise on Scurvy* in 1753. However, it was only in 1795 that the Navy introduced fresh oranges and lemons into the diet of its sailors (Baugh, 1965).

This story, and especially the delay in the implementation of well-known results, has been widely used to illustrate the common delay between research results and their application. It has become a standard example in the literature. But proponents of the case also argue for a number of different conclusions. Herbert Spencer, the 19th Century father of Social Darwinism, a proto-libertarian and sometime beloved of George Eliot, claimed that the story of scurvy demonstrated the ineffectiveness of government and its bureaucracies (Spencer, 1887). More recent medical historians declare that the delay was because, "Surprisingly, the Navy took no notice of Lind's results" (Coleman, 1985:94). Still others, like Jonathan Lomas, a Canadian with an interest in knowledge transfer, assert that this was an early example of continuing resistance of practitioners to apply the results of scientific research - a case of poor knowledge transfer (Lomas, 2002). Examining the historical context and the texts of the time refutes each of these arguments and leads to surprising conclusions that can help us understand the delay, but more importantly can lead us to a richer and more complex understanding of the values and limitations surrounding evidence, the constituents of clinical knowledge and the application of research to practice.

In Lind's day, scurvy was a hot scientific issue. Thousands of sailors of many nations had died of the disease since the beginnings of the age of exploration. The well known nature of the problem of scurvy led many of the finest minds of the day to provide theoretical frameworks for a wide variety of ineffective treatments – including several of the alternatives Lind used in his trial.

In his book, one can decipher the framework that Lind and many others used to try to understand the disease and what might cause and cure it. Lind was a recently trained "modern" physician who had rejected Galenism and adopted the more current chemical-mechanical understanding of the workings of the body. For him, food is normally taken in and processed by the digestive tract into blood and a variety of excreta including urine, stool and perspiration. He believed that in cases of scurvy this digestive mechanism became defective. A severe blockage in the pores of the skin did not allow for proper perspiration, hence the system backed up, the blood putrefied and the symptoms of scurvy emerged. These included blackening of the skin, severe constipation, and extreme lethargy. The smooth functioning of the system could be interrupted by a variety of factors including improper diet, poor air quality and lack of physical activity. And these were the conditions faced by ordinary sailors on long voyages. (It should be pointed out that ships' officers, who had more fresh food, lived in drier quarters, and wore cleaner clothes, had a significantly lower incidence of scurvy and a vastly lower mortality rate from it.)

Lind did not think of scurvy as a deficiency disease as we do. Like others of his day, he sought a cure that would unblock the system or prevent it from being blocked. He saw it not as a lack of some substance, but rather as a result of one or more external causes. In fact, it was only in the late 19th Century that our current notion of deficiency diseases, like scurvy, emerged, and only in the early 20th Century that a lack of Vitamin C was identified as the culprit.

After he describes his clinical trial, Lind declares the efficacy of oranges and lemons in the treatment of scurvy but,

> As oranges and lemons are liable to spoil, and cannot be procured at every port, nor at all seasons in equal plenty and it may be inconvenient to take on board such large quantities as are necessary in ships for their preservation from this and other diseases the next thing to be proposed is the method of preserving their virtues entire for years in a convenient and small bulk. It is done in the following easy manner. (Lind, 1753:156)

And our heart stops as Lind goes on to describe in great detail a process of heating the juice in a glazed earthen basin to almost boiling to allow the water to evaporate and produce a thick syrup (called "rob") that can be reconstituted at sea. In this way the "virtues of twelve dozen of lemons or oranges may be put into a quart-bottle, and preserved for several years" (Lind, 1953:157).

We now know that boiling citrus juice for many hours severely reduces the amount of Vitamin C in the resulting syrup, and the reconstituted juice significantly dilutes whatever is left. It would not, and indeed did not, prevent scurvy. But this "rob", rather than fresh oranges and lemons, was Lind's clear recommendation in his book.

Although it was one among many, Lind's book was a best seller for its time. It was widely circulated, translated into other languages and printed in three editions over the next 15 years. It made Lind's reputation, and, when the Navy built an enormous hospital at Haslar devoted to treating sailors, Lind became its first director despite the failure of his "rob" to be effective. He held this post quite honorably and continued to experiment with the sailors who came there until he retired, whereupon he was succeeded by his son.

There is strong evidence that the Admiralty tried Lind's cure. In a letter to another physician who proposed citrus juice, the Admiralty said,

> The remedy proposed …is not new. Trials have been made of the efficacy of the acid of lemons in the prevention and cure of scurvy on board several different ships which made voyages around the globe at different times, the surgeons of which all agree in saying the rob of lemons and oranges were of no service, either in the prevention, or cure of that disease. (Carpenter, 1986:94)

The situation did not improve between the first publication of Lind's Treatise and its third and final edition in 1772. For example, deaths due to scurvy and other diseases far exceeded the number of battlefield deaths during the Seven Years War. The numbers recorded in the annual report of 1763 declare that of 184,893 men were in the navy, 133,708 died "of diseases and missing" and only 1,512 were "killed in engagements and by accidents" (*The Annual Register, or a View of the History, Politics, and Literature, For the Year 1763*, 1790:50). Once more the pressure for a cure increased, and sea trials continued without any clear success.

As the pressure for a cure for scurvy increased, Captain James Cook organized his first expedition to circumnavigate the world in 1778. He demanded and received every contemporary support for the control of scurvy: ample supplies of Lind's concentrated juice, large stores of fresh and preserved fruits and vegetables, and a careful selection of crew. Cook stopped as frequently as he could to refresh the ship and provide the men with fresh food. The result was the first truly successful voyage in health terms: no one died of scurvy; although the disease did occur when there were particularly long stretches away from shore. Cook made his reputation and received the Copley medal from The Royal Society for his success in staving off the disease (Bown, 2003:166).

Cook's success was followed by intense scientific wrangling. Rivalrous explanations of Cook's success were led by Sir John Pringle (1707-87), the then head of the Royal Society. Pringle reviewed the surgeon's records, and with a strong bias concluded that sweet wort was the most effective preventive of scurvy. This turned out to be a major obstacle to the Navy's acceptance of other solutions, and became the treatment of choice for a number of years, though it was of little value (Carpenter, 1986:17).

It may be worth pointing out that Pringle was not alone in putting obstacles in the way of a solution. The scientific research establishment from his time to the early 20th Century hindered rather than helped the prevention of scurvy. Researchers and scientists naturally apply successful solutions from one area to another. However, they are often so committed to their settled frameworks that they press for favoured solutions in the face of massive evidence to the contrary. The greater their authority, the more resistant they seem to be to new ideas. Occasionally their intransigence is even harmful. The history of scurvy is rife with such examples. Pringle was, himself, not only President of the Royal Society, but a Copley medalist. He associated scurvy with rotten foods and believed in giving sailors foods such as sweet wort that would ferment in the stomach and correct the problem. Later, other figures such as Sir Robert Christison (1797-1882) President, British Medical Association and physician to Queen Victoria, Jean-Antoine Villemin (1827-92) of the French Academy of Medicine, William A. Hammond (1828–1900) U.S. Surgeon General, and even Lord Lister (1827–1912), advocated dramatically false or misleading views about scurvy (Carpenter, 1986).

In the face of the medical establishment, progress could still be made on the policy front. Gilbert Blane, a physician from an upper class family, joined the navy in 1781 as Physician to the Fleet. From this position he had privileged access to the Admiral. After a short time he wrote that scurvy "may be infallibly prevented or cured by fresh vegetables and fruit, particularly oranges, lemons or limes" (Carpenter, 1986:92). His early letters to the Admiralty did not overcome the obstacle based on the superior scientific authority of Pringle. However, he persevered, and in 1793 he instituted a fresh test on one ship with the help of a friendly Admiral. Each man received two-thirds of an ounce of lemon juice mixed into the daily ration of grog. The ship took 23 weeks to reach India without touching land. Several men showed some symptoms of scurvy, but those soon disappeared after an increased dose of lemon juice. By the time the ship reached Madras, no one was affected by the disease.

In 1795, soon after Blane became a Commissioner on the Board of the Sick and Wounded Sailors, the Board recommended a daily allowance of three quarters of an ounce of lemon juice as part of the daily ration. After this date, the incidence of scurvy dropped very quickly. Just as the poor health of sailors due to scurvy was thought by some historians to be a factor in the British loss during the American Revolution, their good health after the elimination of scurvy was considered to be a major factor in the British maritime victories during the Napoleonic Wars (Porter, 2002).

Throughout the 19th Century, scurvy reappeared in various forms. It was rife among army troops who spent long winters away from fresh food. It was misdiagnosed for years when middle class infants were fed scientifically developed formulaic substitutes for mother's milk (Carpenter, 1986). It even reappeared in the Royal Navy when dilute lime juice with little ascorbic acid was widely substituted for the real thing.

It was only in the 19^{th} Century that the notion of deficiency diseases with an accompanying need for special substances to sustain the smooth functioning of the body was introduced. This required making a distinction between food that functions as fuel to keep the body running, and special additional substances that keep it running smoothly. It is much like the distinction between gasoline and the additives that keep the car engine from knocking. At first these additives were called the "vital amines", and this became shortened to "vitamins" even though they are not amines. And when Vitamin C was isolated, it was called "ascorbic" acid precisely because it was the vital substance needed to avert scurvy.

A research-based understanding of the disease was delayed until the early 20^{th} Century even though there was an understanding of deficiency diseases well before then. One reason for this delay was that scurvy did not fit the model of germ-caused infectious diseases which were the focus of attention for most of the latter part of the 19^{th} Century. Sir Almroth Wright, an important figure in immunology, and the founder and chief of the laboratory where penicillin was discovered, is best known for his work on typhus. His reputation was so great that he was also widely considered to be an authority on scurvy.

The thirteenth edition of the Encyclopedia Britannica, published in 1911, continued to declare the uncertainty surrounding the causes of scurvy and even advocated several more "elemental" cures including those of Wright – all of which would have been totally ineffective.

> The precise etiology is obscure, and the modern tendency is to suspect an unknown micro-organism; on the other hand, even among the more chemical school of pathologists, it is disputed whether the cause (or *conditio sine qua non*) is the absence of certain constituents in the food, or the presence of some actual poison. Sir Almroth Wright in 1895 published his conclusions that scurvy was due to an acid intoxication, …..Wright has proposed giving what he terms anti-scorbutic elements (Rochelle salt, calcium chloride or lactate of sodium) instead of raw materials such as lime juice and vegetables, as being more convenient to carry on voyages.(*Encyclopedia Britannica*, 1911:517)

The credit for the understanding of scurvy is most appropriately assigned not to medical researchers, but to two nutritionists, Axel Holst and Theodor Frölich, working in Norway who described an animal model of scurvy in guinea pigs in 1907. Once an animal model was found, Vitamin C was isolated by Albert Szent-Geörgyi, a Hungarian scientist working in Cambridge. He received a Nobel prize for this discovery while the nutritionists were ignored (Moss, 2007).

Vitamin C is an excellent example of a "magic bullet." For people who are suffering from scurvy, even small amounts of Vitamin C act as a rapid, even a miraculous cure. However, not all diseases are like either small pox or scurvy. In fact, our notions of health and disease continue to change. Most recently, powerful computers have enabled us to track a wide range of variables relevant to health, including ones about our genetic makeup, our social status and our physical environment. We have increasingly found that health is a result of the interactions among them and that chronic diseases have especially complex etiologies: they can take a wide variety of courses. Prevention and treatment of such widespread conditions as type 2 diabetes, child asthma and clinical depression are increasingly leading us away from the search for magic bullets like Vitamin C and toward a combination of lifestyle, nutritional and environmental interventions that either substitute for or are used in conjunction with varying amounts of multiple medications.

This increased complexity has led us in an entirely different direction. It creates difficulties for universal solutions in many areas, not only for chronic diseases. This has made it more difficult to standardize the recommended daily requirement for Vitamin C. Although a small amount of Vitamin C is needed to avert scurvy, all countries recommend more than that amount. However, there is no agreement about the amount of Vitamin C needed to maintain general health or to respond to chronic conditions such as heart disease or cancer. Nor is it clear that such amounts can be easily standardized. Different countries have set requirements that have varied by as much as 100% because in each country scientists have come to a different consensus. Their disagreements are at least partly based on the gradual realization that the amount of Vitamin C that is needed will vary between individuals over quite a large range depending on psychosocial and environmental factors, as well as purely physiological ones.

It is well worth summing up and making explicit some of the lessons from this revised version of the scurvy story.

1. It is now widely accepted in Philosophy that the evidence-based true-belief model of knowledge is not quite foolproof. The case of Lind is a good example of this. Lind had the evidence that oranges and lemons cured scurvy. He was justified in the true belief that they did so. Unfortunately he concluded that the "rob" made of concentrated juice would effect the cure for scurvy. And so we cannot conclude that he *knew* what the cure for

scurvy was. We have also learned that his conclusion was transferred into practice without effect. We can infer from this case, as in many others, that what was transferred was not knowledge, but an evidence-based mistake.

2. Research problems are understood in a theoretical frame. At times, because the frame is undergoing change, or is incomplete or wrong-headed, it can lead researchers away from a viable solution. There can be lots of evidence for a conclusion within the frame, but the conclusion can still be mistaken. This can happen even when a solution is staring them in the face. Lind's trial was incredibly successful and yet failed to provide a practical solution. He framed the disease as a blockage of the digestive tract and this suggested to him that unblocking it probably was connected to the acidic content of the juice. Even if he further concentrated the acid in the fresh orange and lemon juice by boiling it, it should still unblock the system. Of course it didn't work, but we can see how he was misled by how he understood the problem.

3. At times the conceptual apparatus for understanding a disease is unavailable. The notion of deficiency diseases was really only introduced in the mid-19th Century. This made it more difficult to conceptualize possibilities and test for them. A good example of this was Cook's success. In hindsight we can see that this was largely due to his frequent stops to "refresh" his ships. At these stops he insisted that the men eat fresh fruits and vegetables. Yet this was overlooked at the time even by such luminaries as Sir John Pringle whose biased reading of the ship's diaries sent him off into a self-serving and wildly mistaken direction.

4. It is likely that the scientific research establishment from the time of Pringle to that of Wright hindered rather than helped the prevention of scurvy. Everything from sweet

wort to sulfuric acid were advocated by prominent scientists and researchers to little or no effect. There is no reason to think that the current scientific establishment is any different; unconventional but possibly productive research continues to receive little to no support.

5. The successful implementation of the orange and lemon juice cure in the British Navy was not primarily the result of scientific research. It was instituted more than a century before scurvy was understood and Vitamin C was identified as the missing agent that caused it. The adoption of citrus juice as part of the British sailor's diet had numerous contributing factors including Lind's book, Cook's voyage, Blane's conviction of its efficacy, not to minimize the importance of his links to the upper class. Perhaps all were consequent on the Admiralty's continuing quest for a solution. Recent epidemiological studies tend to point towards a complex series of factors (at times wrongly called "determinants", but that is for another paper) that can play a role in turning around population health problems. There is growing agreement that these changes are often not merely the result of the application of scientific research. The reduction in general mortality in the 19th Century, and the reduction of tuberculosis in the 20th Century, has been attributed to increased wealth, better housing and other socio-economic measures rather than to medical breakthroughs.

6. Finally, even when we understand the disease, and the magic bullet that cures it, we remain unclear about other related issues. For example, there is no settled view about the daily dose of Vitamin C. How much do we really need for a healthy life? The recommended daily dose of Vitamin C varies from country to country and from researcher to researcher. This might be because there is no standard amount. We probably

need differing amounts of it depending on a wide range of variables, sometimes called determinants of health. Because these interact with each other in complex ways, there is more than likely no single answer to this question.

These lessons may not all be generalizable, but they do suggest that we should examine the path from research to application more carefully for it can be far more complex than we first think. A large number of variables can have an influence on this transition and many can be unforeseen. The story of scurvy also demonstrates that scientific preconceptions can impede as well as help research. It is a palpable example about the impact of scientific power and politics on what counts as acceptable scientific research in any period. All of this suggests a complexity that is ineradicable in the accumulation of knowledge and in the application of what we have learned.

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