An Introduction to Nutritional Medicine

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Where Darwin Meets Hippocrates

By

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Cambridge Scholars Publishing

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PREFACE

Thirty years ago, I decided that there was a significant gap in my knowledge base as a GP (general medical practitioner or family doctor) and I embarked on a course of education that included a degree in Nutritional Medicine at the University of Surrey. More recently, I have been able to research the attitude of my fellow GPs on nutrition science and Nutritional Medicine. Although the scepticism of the 1980s has given way to a more open-minded attitude, there is about as much confusion on issues such as alcohol, veganism and dietary fats amongst GPs as there is amongst members of the general public. In 2019 Cambridge Scholars Publishing published my book "Nutrition and Science – a Darwinian perspective on Nutritional Medicine" which was an attempt to deal with the confusion on this subject. I made the point that much of this confusion is unnecessary. However, it is a large book and, unavoidably, included a fair amount of technical language. This new book is an introduction to Nutritional Medicine and it is shorter and almost completely shorn of technical language. However, I have again attempted to deal with the confusion amongst GPs and their patients. I have always found Charles Darwin very helpful when trying to judge such issues and I have developed the scientific philosophy of the three strands of proof (body chemistry, observational research and scientific trials) against the Darwinian backcloth.

2½ thousand years ago, the great Hippocrates warned patients and colleagues not to be too dependent on medicinal remedies (mainly herbal back then) and stated 'Let food be thy medicine and let medicine be thy food.' Undoubtedly, he was the first significant champion of Nutritional Medicine. This made me wonder what would happen if Darwin and Hippocrates were to meet – somewhere in heaven, perhaps. They would undoubtedly find they had a lot in common. Hippocrates came from a family of doctors and both his sons followed in his footsteps and Darwin also came from a family of doctors and started at medical school but, luckily for science, changed course. Therefore, I have started each chapter with an introductory dialogue between Darwin and Hippocrates.

I would like to pay tribute to all the members of the Department of Nutrition Science at the University of Surrey who have helped me with my writing and research but especially Joe Millward, Margaret Rayman, Susan

Lanham-New, Michelle Dobrota Gibbs, Bruce Griffin and Barbara Engel. I have learned a lot about diet and the microbiome from Glenn Gibson at the University of Reading and about nutrition and the brain from David Smith at the University of Oxford and Michael Crawford at Imperial College, London. Most of what I know about food allergy and intolerance has been acquired from attending meetings of the British Society of Ecological Medicine whose president Damien Downing has been a good example of forthright independence of mind. I would also like to thank the many GPs and practice managers in the Guildford area (too many to list) who have collaborated with me on research projects. I am very grateful to Professor Paul Grob who has encouraged me to press on with this research and to my wife, Tina Nichols (retired hospital pharmacist) for reading through my manuscript and suggesting improvements and corrections. Lastly, I would like to thank the staff at Cambridge Scholars Publishing for helping me to get my ideas into print.

Chapter 1

Is Nutritional Medicine based on science?

Hippocrates meets Darwin

Two old fellows sat on a comfortable bench on a hillside admiring the emerald vista of a landscape of woodland and meadows. The sun was high in a clear blue sky but a half-grown mountain ash provided shade, and a gentle breeze eased the noonday heat. They looked as if they could be brothers. Both had white hair, full beards and receding hair and similar facial features. However, one of them had a shorter beard and his hair curled. He was the Greek. The other was English.

They had arrived at the bench separately and sat together without a word for all of five minutes. Then the Greek gentleman broke the silence with an observation, 'What a wonderful view'.

The Englishman, who had a reputation in his lifetime for being reserved and often preferring his own company, hesitated. He may have been reserved but he was always polite and basically kind hearted. His new companion had spoken in Greek, a language he had learned at school and university. 'Yes indeed, a beautiful landscape. Please excuse my Greek. It is not so good'.

They soon established that their only common language was Greek and the Englishman found that memories of the language that had been hammered into him as a boy, without any apparently good reason, came flooding back. Soon they were talking together like old friends and the Englishman was describing the enormous variety of life hidden within the woods and meadows before them.

The Greek pointed to the East and explained, 'I come from a village on that purple hill but you can't see it from here. They call me Hippocrates, physician of Cos'.

‘Good gracious, not ***the*** *Hippocrates from the time of Pericles?’*

‘Yes, that’s me.’ He smiled

‘I am most honoured to meet you in this ...’, The Englishman hesitated again,‘....this strange location - wherever we are. My village is right over there’, He pointed west, ‘Just beyond the river and my name is Darwin, Charles Darwin. I am an Englishman’.

‘An Englishman, I don’t think I know that’.

‘Sorry, I should say that I come from Britain but a long time after your era. It’s very strange to meet you like this’.

‘Do you think this is some sort of afterlife?’ said Hippocrates, ‘It doesn’t seem like Hades’.

‘Perhaps more like Heaven’, said Darwin, ‘That is a sort of idyllic afterlife as described by a Jewish sect a little after your time. But I gave up on religion, so I don’t believe in Hades or Heaven, but this.....’

‘Difficult to explain’, said Hippocrates.

‘Very difficult’, said Darwin.

They sat in silence for a while. A passing wasp circled them, landed on Darwin’s bare arm and investigated it whilst Darwin glanced down briefly but stayed motionless. After a minute, the wasp gave up and flew on across the hillside.

‘I started to learn your trade’, said Darwin, ‘But I gave up after a year or so. There was too much blood and guts, and cruelty. Well, that was my experience anyway’.

‘I’m sorry to hear that’, said Hippocrates, ‘Cruelty shouldn’t happen in my trade but it’s always a possibility. You know that I believed that even slaves should be shown kindness and respect’.

‘My wife was a great champion of slaves and their rights’.

‘So, what did you turn to after medicine?’ asked Hippocrates, ‘No, don’t tell me. It was the study of your beloved plants and animals wasn’t it? Just like my young friend Aristotle’.

'It's true. I devoted my life to the natural history of plants and animals. I travelled right round the world then wrote many books about my travels and researches and most important of all about where all the plants and animals and people came from. My theory was that there is a great family tree of life and that many millions of years ago, the first living things were created and everything else came from them. According to my family tree of life, our nearest relatives are the great apes and the monkeys are slightly more distant relatives. That idea upset the priests and religious people and got me into a bit of trouble'.

Hippocrates shook his head in amazement. 'That is quite a revolutionary idea my friend and I'm not surprised that it made you a little unpopular. Don't worry though, I like new ideas. As for me, my suggestion that healing could be done without the interference of priests and religious rites got me thrown in prison for twenty days.

'Now, with your theories about the true nature of life and my observations on food and health, I think we should be able to find some interesting ideas to discuss but perhaps another day. From the lengthening shadows I can see that it is time for me to return to my village. Perhaps we can meet again tomorrow.'

'I look forward to that' said Darwin, 'same time, same place?'.

* * * * *

Where does Nutritional Medicine fit in?

Hippocrates is thought to have been sceptical about the overuse of herbal remedies. He said: 'Let thy kitchen be thy apothecary; and let foods be thy medicine'. Of course, neither he nor Darwin knew about vitamins, let alone the importance of trace elements like selenium and zinc. Despite this there are many interesting parallels between the ideas of Hippocrates and our own ideas and it is no accident that Hippocrates and Darwin find that they have a lot to discuss. I wonder what Hippocrates would have thought of vitamins and vitamin takers. His aversion to raiding the apothecary's pot when a healthy diet would be a better and more natural remedy might be a clue. But perhaps the truth of the matter is not quite that simple.

Late 20th Century medicine supplied two easy answers to patient's questions about nutritional supplements – too easy, unfortunately, to be adequate:

1. *If it's a natural substance, it might not do you much good but it can't do you any harm.* Although there is some truth in this when referring to a modest dose of a vitamin, for instance, we now have evidence that higher "pharmacological" doses of vitamins like vitamins E, A and B6 might be harmful in some circumstances, but the evidence is inconclusive. Since herbal remedies are sometimes referred to as supplements, every GP will realise that herbs like St John's Wort are more like drugs, with side effects and the potential for interaction with other drugs.

2. *You don't need to take extra vitamins and minerals if you eat a well-balanced diet.* This is a gross oversimplification. We now know that even the best, most varied, Western diet is not the same as the stone-age diet that we are adapted to as a result of millions of years of evolution. This is especially true of the low vegetable fibre content of modern diets. Added to this, many of our patients have psychological and money problems that prevent them from eating well. Nearly all food surveys show that 20-30% of people in the UK never eat fish, and some will tell you that they find the very thought of it disgusting

3. Another easy answer is to tell patients with normal IgE blood test (immune globulin E) and the related allergy tests that "….food allergy is all in the mind". We now know that this is not necessarily the case. For instance, some patients with irritable bowel syndrome (IBS) can tell you exactly which foods exacerbate their symptoms although they do not test positive on any standard type of allergy testing. The balance of evidence from dietary studies suggests a rule of halves:

   ❖ Half the patients who think they have a "food allergy" but have normal IgE and RAST (radioallergosorbent test) will have a genuine food intolerance and half will be imagining it.

   ❖ Half the patients with a genuine food intolerance will have some idea what foods are problematic and, with minimal help and understanding, they will be able to control their symptoms.

Primary care practitioners have another problem that has developed over the last 20-30 years. Patients really would prefer a natural remedy to a drug if this was available and, increasingly, this is an option. Table I represents the arguments for and against the practice of Nutritional Medicine in primary care and Table II compares it with pharmaceutical drug-based medicine and the related disciplines of Herbology and Homeopathy.

However, a substantial proportion of medical decisions and self-treatments are carried out in the community without consulting a doctor (Figure 1). I was surprised how many when I first saw this diagram! Obviously, however, these are mainly minor matters like taking pain killers for arthritis or a headache or getting over-the-counter treatment for hay fever. Mothers may decide that a bleeding scalp wound acquired in a "play fight" is not bad enough for a doctor's opinion and deal with it quite adequately themselves and there are plenty of home remedies for chilblains, mouth ulcers etc. A significant proportion of self-treatment decisions involve natural remedies purchases over-the-counter involve nutritional supplements, homeopathic remedies and herbal remedies. Orthodox medicine rejects many of these remedies

Table I. Comparison between Orthodox Medicine and Nutritional Medicine

	Orthodox medicine	Nutritional medicine (NM)
Main emphasis	Involves understanding physical, social and psychological components of disease and usually a pharmaceutical solution but lifestyle advice is relevant	More emphasis on the physical component with an analysis of allergy, environmental and nutritional factors unique to the individual
Suitability to primary care environment	Usually fits into seven minute consultation and the computer software is designed for the orthodox approach	May take longer than seven minutes and NM repertoire (prescription items and tests) is seriously incomplete in the computer software
Patient preference	Many patients would prefer to avoid pharmaceuticals. They will often, however, opt for a "quick fix" if a pharmaceutical can do this	The NM approach with advice on diet and supplements may be preferred, as long as it is not too complex
Side effects	Common	Rare

Figure 1. Proportion of medical decisions made by patients without seeing a doctor compared with GP consultations and referrals by the GP for hospital treatment (hospital treatment is more likely to involve life-saving procedures)

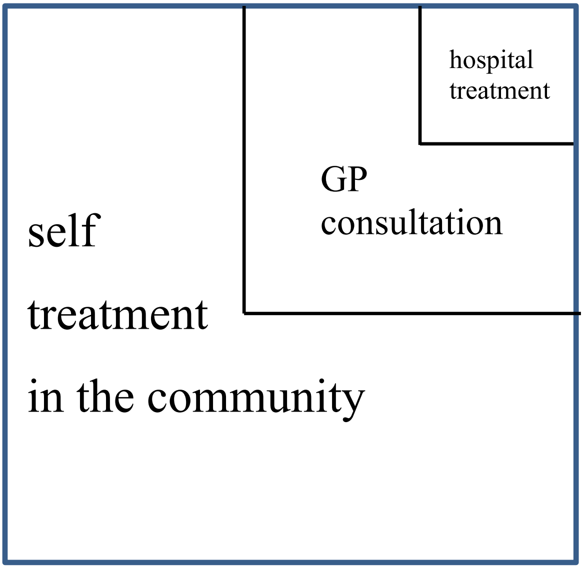
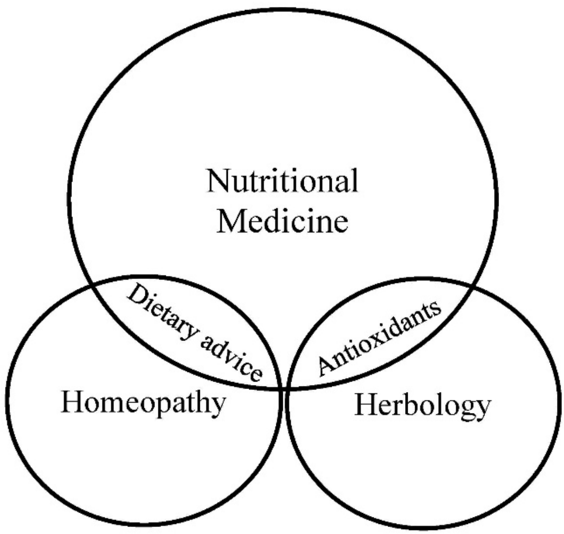


Table II. Comparisons between Nutritional medicine and other disciplines

	Basic mechanism	Efficacy	Side effects
Pharmaceuticals	Usually achieves a favourable effect on body chemistry by blocking or "poisoning" an enzyme system	Rapid and reliable for short term effects and commonly life-saving	Common, usually reversible but occasionally lethal
Nutritional medicine	Optimum nutrition is rarely achieved and therefore nutritional status can be manipulated to cure or prevent disease	Longer interval from treatment to beneficial effect but a nutritional regimen may be more likely to offer a long-term solution	Side effects are rare at nutritional doses and most micronutrients and nutraceuticals are only toxic in much higher doses (c.f. vitamin A)
Herbology	Remedies based on hundreds of years of trial and error and usually contain a mixture of nutritional and pharmacological properties	May be very efficacious, but trial evidence is often poor or incomplete	Common, as with pharmaceuticals, and this is one reason for a UK directive in 2005 on registration of "Medicinal Herbals"
Homeopathy	Not scientifically established but current theory involves modification of water molecules by succussion and serial dilution	Unexpected evidence for efficacy from double blind RCTs, but this has been challenged on the basis of trial design	None. This is the main "selling point" in favour of homeopathy, but homeopathic practitioners will often also prescribe pharmaceuticals, herbs and NM

Figure 2 shows how the non-orthodox disciplines overlap. In the overlap areas are dietary advice (where Nutritional Medicine overlaps with Homeopathy) and antioxidants (where nutritional medicine overlaps with Herbalism). Antioxidants are natural substances that mop up free radicals. Free radicals are small highly reactive molecules that are released by normal metabolism and released in larger quantities by smoking, alcohol and some other illegal drugs and an excess of antioxidants can cause disease and accelerate ageing. Nutrients with antioxidant properties include vitamins A, C and E and lycopene (the red pigment in tomatoes) and they may also be present in herbs. Green tea is a good source of the antioxidant catechin. The antioxidant quercetin is present in onions and in a wide range of herbs including fennel and watercress. Turmeric, a key ingredient in curry powder, contains the antioxidant curcumin.

Figure 2. Areas where the three disciplines, Nutritional Medicine, Homeopathy and Herbology overlap



Interpreting the evidence

How do we decide which school of thought to believe and which research to believe? This requires scientific thinking. 2½ thousand years ago Hippocrates introduced a scientific way of thinking about health, disease and prevention of disease that most of us take for granted. He emphasised the importance of observing and recording the medical history and clinical examination of patients and using this material to draw general conclusions. He noted, for instance, that the passage of black digested blood in the motions was usually a sign that the patient was going to die. I should quickly add that nowadays it would be interpreted as a sign of internal bleeding which is a surgical emergency but with a favourable outcome! Hippocrates rejected supernatural explanations for disease and put the emphasis on physical explanations. Of epilepsy, which was believed to be a sacred state of mind caused by the gods, he wrote: ‘I do not believe that the "Sacred Disease” is any more divine or sacred than any other disease but, on the contrary, has specific characteristics and a definite cause.’ However, extensive and impressive his observations were, there is no record that either he or his contemporaries carried out medical experiments. This is surprising as new treatments must have been introduced and tested at some stage. I find it difficult to believe that new treatments were never tested out on slaves.

Figure 3. Development of scientific thinking from time of Hippocrates to 20th century

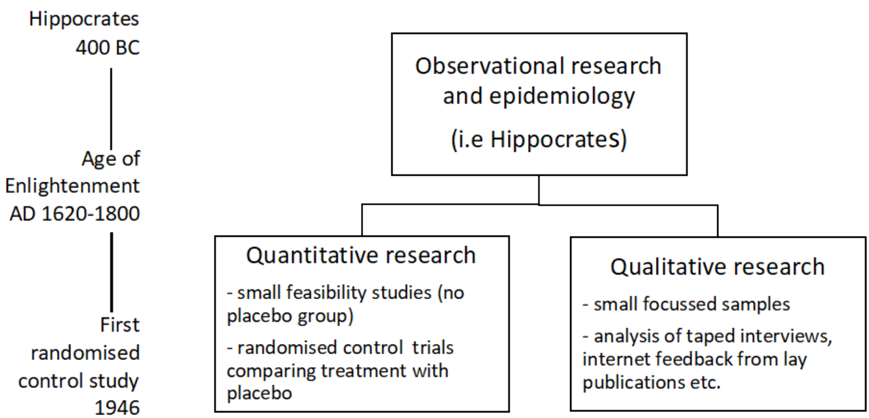
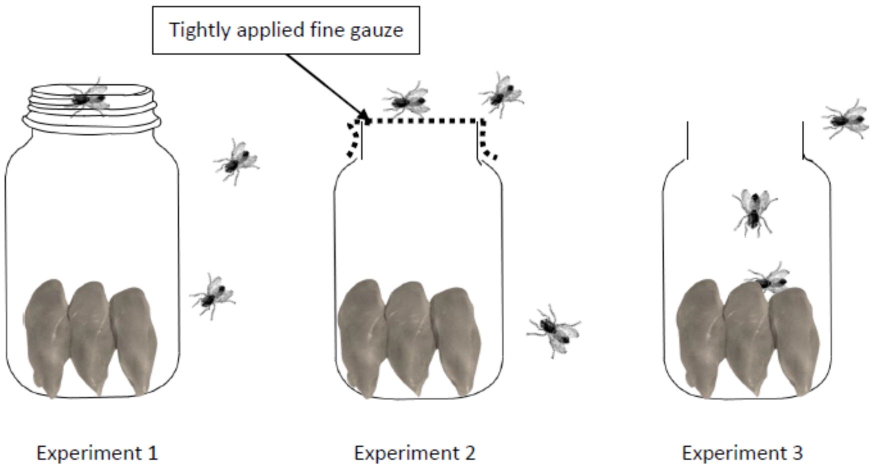


Figure 3 shows how different types of medical research have evolved starting with Hippocrates who was not only the father of clinical medicine but also the father of medical epidemiology. He travelled widely around the ancient world making observations on lifestyle, diet, geographical location and health. He noted, for instance, that high alcohol consumption where the diet was poor was associated with a variety of health problems. Subsequently, there was very little change until the age of enlightenment despite the work of famous “observers” such as Galen, Avicenna and Paracelsus until the Age of Enlightenment when experimental science took root and finally led to the randomised control trial which is today’s “gold standard” of quantitative research (i.e. research that involves counting). However, qualitative research is playing an increasing role and this depends upon analysing a relatively small sample in greater depth.

Figure 4. Francesco Redi carried out a series of experiments to determine how maggots are generated in rotting meat



However, scientific experimentation never really progressed significantly until the 1620s AD although I suspect the work of many laterally thinking innovators has been lost in the mists of history or simply suppressed and destroyed by conservative orthodoxy. The first ever controlled experiment that we know of was by an Italian – Francesco Redi. He published his finding in 1668.

He carried out a series of experiments with open and closed jars containing perishable foods such as fish and meat. These are summarised in Figure 4 in which all three jars contain chunks of raw venison. In experiment 1, in which the lid of the jar was closed, there were no maggots. If the jar was open, as in experiment 3, maggots developed and Redi noted that flies entered the jars and laid eggs on the venison. In experiment 2, a fine gauze was firmly applied to the mouth of the jar. Redi noted that flies landed on the gauze and despite being unable to get to the venison, they laid eggs on the gauze that hatched into maggots which soon died. Aristotle, the Greek philosopher, was revered throughout the medieval and renaissance periods and he subscribed to a commonly held belief in spontaneous generation of life from "putrefying matter." Like Hippocrates, Aristotle was a great observer of nature but unlike Redi and other luminaries of the age of enlightenment, Aristotle never carried out experiments to test his ideas and nobody seriously doubted the pronouncements of the great man until Francesco Redi came along. Even then, the theory of spontaneous generation of life from mud, slime and putrefaction was largely uncontested until the early 1800s.

The origins of germ theory of disease are lost in the mists of history but it was certainly being discussed in the 1600s. The theory was rejected by the vast majority of medical practitioners and early scientists. However, in 1676 the Dutchman Antonie van Leeuwenhoek developed the first microscope and was able to identify bacteria and many other microscopic structures. He corresponded with the Royal Society in London who initially doubted his scientific integrity but eventually accepted his findings. In 1857 the researches of Louis Pasteur finally replaced the theory of spontaneous generation and validated the germ theory of disease. Pasteur carried out a series of experiments that were similar to Redi's experiments (Figure 4). He proved that microscopic life-forms in the air are responsible for putrefaction and fermentation (bacteria and yeasts). Subsequently Louis Pasteur and the German physician-scientist Robert Koch were able to further develop the germ theory of disease. Koch laid down a set of criteria for establishing the link between a disease and microorganisms known as Koch's postulates:

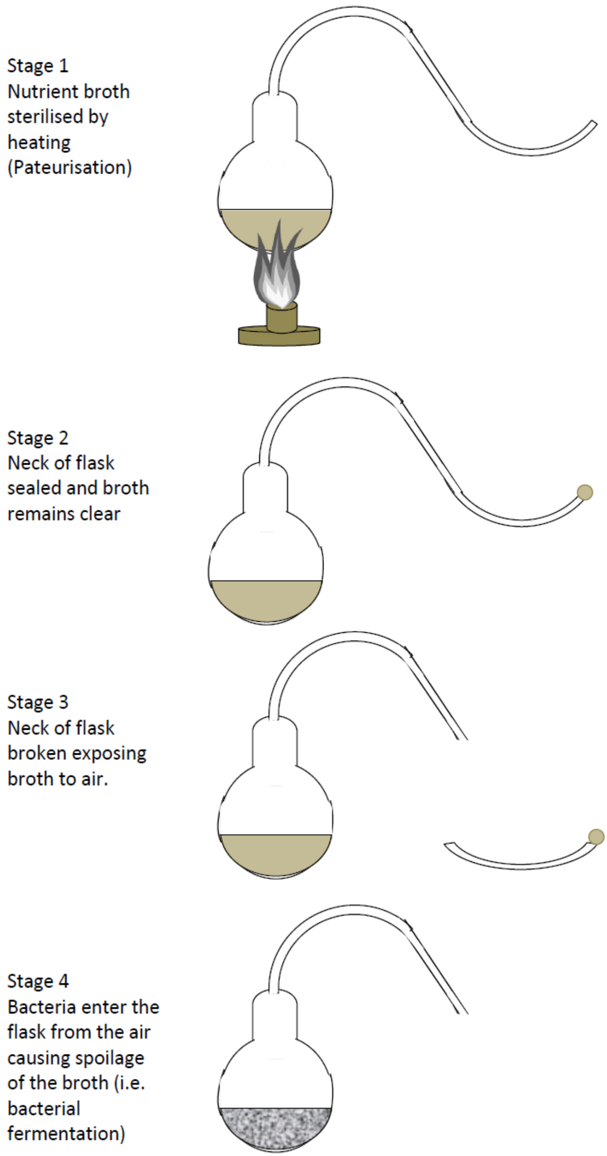
1. The microorganism must be found in abundance in all organisms suffering from the disease, but should not be found in healthy organisms.

2. The microorganism must be isolated from a diseased organism and grown in pure culture.

3. The cultured microorganism should cause disease when introduced into a healthy organism.

4. The microorganism must be re-isolated from the inoculated, diseased experimental host and identified as being identical to the original specific causative agent.

Figure 5. Louis Pasteur showed that a nutrient broth sterilised by heat will not undergo bacterial fermentation until it is exposed to micro-organisms



Who discovered vitamins?

This theoretical framework (paradigm) was almost immediately used to determine the disease processes in anthrax, syphilis, tuberculosis, rabies and cholera. However, not all disease is due to pathogenic microorganisms and mistakes were made. In 1804, Japanese doctors gave the first detailed description of kakké which is better known as beriberi. The condition starts with creeping paralysis of the legs, then swelling of the lower extremities and finally heart failure and death and was particularly common in the Far East in institutionalised populations such as military and prisons. Beriberi was becoming a problem for the Dutch authorities in the Dutch East Indies. The important breakthrough came in 1890 with a young army surgeon, Christiaan Eijkman, who was researching beriberi in Java using various animal models. The research was based on Koch's postulates and involved injecting animals with bacterial cultures from the blood of human beriberi subjects. He found that the chicken was a good animal model for beriberi but that there was little difference in the severity of chicken beriberi between those injected with the bacterial culture and those who had not been injected. Then, to his amazement all his chickens suddenly recovered from the disease. However, the clue was a change to the chicken feed and this was something that Eijkman's assistant organised. Normally, the chickens were fed on a standard feed grade uncooked brown rice but unbeknown to Eijkman, the assistant had acquired leftover cooked white rice from the cook at a neighbouring military hospital for a period of five months. However, when a new cook took over, he refused to continue the arrangement. The miraculous return to good health of the chickens coincided with a return to standard brown rice chicken feed. Once Eijkman's assistant "came clean" and explained this, a new avenue of research opened up. After carrying out a series of experiments, Eijkman realised that there was a substance in the outer layer or "silverskin" of the rice grain that was "indispensable to life and health" but which would have been completely removed in the polishing process that is used to produced white rice.

Subsequent efforts to isolate this special substance culminated in the work of Casimir Funk 22 years later in 1912. Although Funk came from Poland, he was researching the anti-beriberi substance in rice silverskin at the Lister Institute in London. He identified and purified an organic compound containing an amine group and since this was a vital substance containing an amine he invented the term "vital amine" which was shortened to "vitamin." We now refer to the vital amine that Funk isolated as vitamin B1 (chemical name thiamine). Like most good scientists, Funk was gifted with a creative imagination and went on to suggest that scurvy and pellagra were also due to vitamin deficiencies and this was soon proven to be true. Thus, an alternative paradigm to the germ theory of the causes of disease emerged. Since we subsequently discovered that trace elements and minerals like zinc, selenium and iodine are essential to life, let us call this the micronutrient deficiency theory of disease as the word “micronutrient” covers both vitamins and trace elements that are essential to life. Although this was a significant paradigm shift, the two theories on causation of ill health are both equally relevant and most certainly not mutually exclusive. For instance, some diseases caused by microorganisms are more likely to take a hold on an individual when there is a micronutrient deficiency such as a vitamin deficiency in an obese child eating a high calorie diet of junk food. This is the meaning of the term “empty calories” – food that is high in calories but lacking essential micronutrients

Once the importance of a micronutrient to good health was established, there was a flurry of activity in the research world. As Funk had predicted, scurvy was found to be due to deficiency of a vitamin that we now call vitamin C or ascorbic acid. It was already established back in the 16th century that something in citrus fruit prevented scurvy in sailors but this finding was forgotten and rediscovered several times. However, the first recorded case of a cure for scurvy was found in an Egyptian papyrus dating from 1550 BC. Dietary treatment with onions was recommended and we now know that onions are as good a source of vitamin C as citrus fruit. Surprisingly, although Hippocrates was aware of the disease and described it in detail, he was unable to find a cure. By 1831 when Darwin started a voyage around the world with Captain Fitzroy in the Beagle, there was a standard issue of lemon juice to all members of the crew and scurvy had become a thing of the past. In 1930 the Hungarian scientist Albert Szent-Györgyi working at Cambridge university, isolated an anti-scurvy acidic substance from adrenal glands and the name “ascorbic acid” was derived from its anti-scurvy (anti-scorbutic) activity. Both Eijkman and Szent-Györgyi received the Nobel prize for science but, surprisingly, Funk did not.

Further research was needed to determine the daily requirement of vitamins and in the case of vitamins A and C some important work was carried out on conscientious objectors during World War 1 who volunteered to take part in these experiments based on the University of Sheffield.

Some aspects of these experiments would never be given serious consideration by a research ethics committee in the UK in the 21st century and although research standards are laxer in some developing countries, I doubt if their ethics committees would pass them either. One experiment, for instance, involved inducing scurvy by feeding a vitamin C deficient diet to 10 volunteers. When classical signs of scurvy such as bleeding gums were established, a 3 cm incision was made in the thigh under local anaesthetic and stitched up with three sutures. Then the subjects were treated with various doses of vitamin C ranging from 0 mg to 70 mg daily. Then, at various stages during recovery from scurvy symptoms (sometimes symptoms were quite severe including heart pain) the strength of the healing wound was tested using weights suspended from the edge of the wound on a hook to test if the wound would break open under stress. This experiment showed that although 10 mg daily prevented scurvy symptoms, 20 mg daily was needed for optimal wound healing.

A paradigm shift

The next important paradigm shift was the invention of the randomised double-blind controlled trial by Austin Bradford Hill in 1948. There were a number of controlled trials carried out in the 1940s including a headache trial by Elvin Morton Jellinek in 1946 that compared three different combinations of drugs with a dummy tablet or what we now call a placebo. However, the best organised and most memorable trial was the British Medical Research Council trial of the antibiotic Streptomycin in treatment of tuberculosis in young patients aged 15-30 years. Austin Bradford Hill was the medical statistician who masterminded the randomised double-blind aspect of the trial. This was a new model for research that involved a statistical method of randomising allocation of patients to either standard treatment plus Streptomycin or standard treatment alone (Figure 6). The trial participants were blinded to treatment or, in other words, they had no idea that they were in a trial or which group they were in.

What was special about Bradford Hill's approach was the recognition that simply allocating alternate patients to the two alternatives (streptomycin or control group) would not rule out the risk of a biased result. This has been shown time and time again. Therefore, allocation of patients to treatment and control group must be absolutely random and various techniques have been developed by statisticians to achieve this. Jellinek had already shown that the placebo tablet containing zero active ingredient can have a small but significant beneficial effect on patients and the combination of Bradford Hill's blinded randomised allocation and a placebo tablet has now become the gold standard for medical research (Figure 5). Nowadays, unlike in 1946, trial participants have to be fully informed which means that sometimes the risk that you might be taking the placebo and not the magical "new drug" can be a cause for concern, especially if this is a trial of a new treatment for a life-threatening condition such as a cancer or a serious neurological condition.

Figure 6. Randomisation of subjects in the 1948 MRC Streptomycin trial

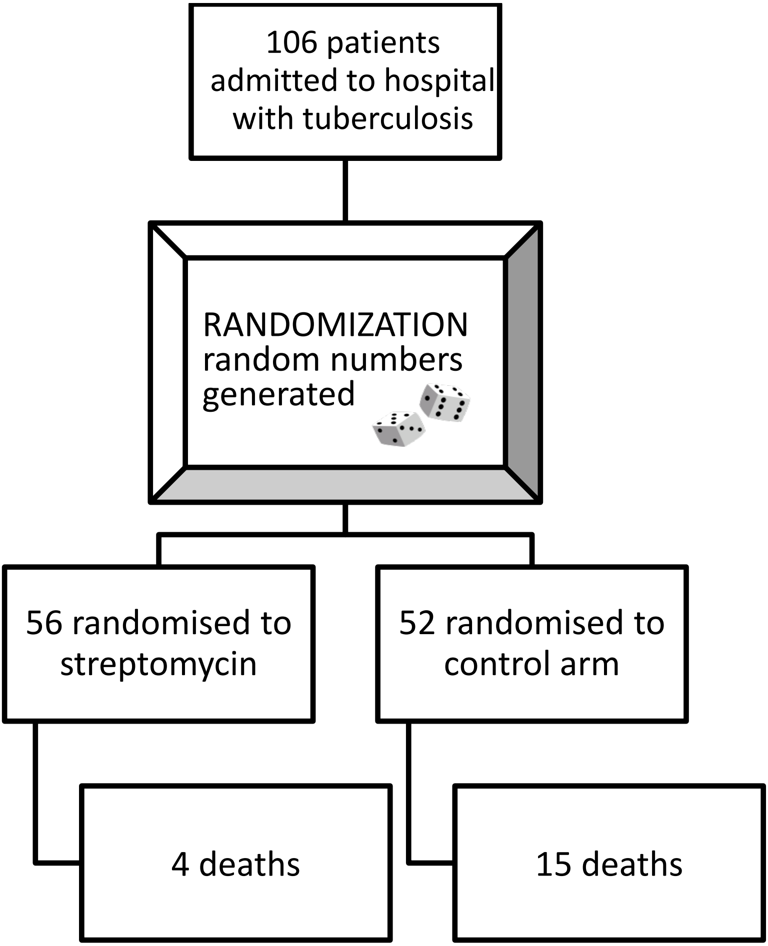
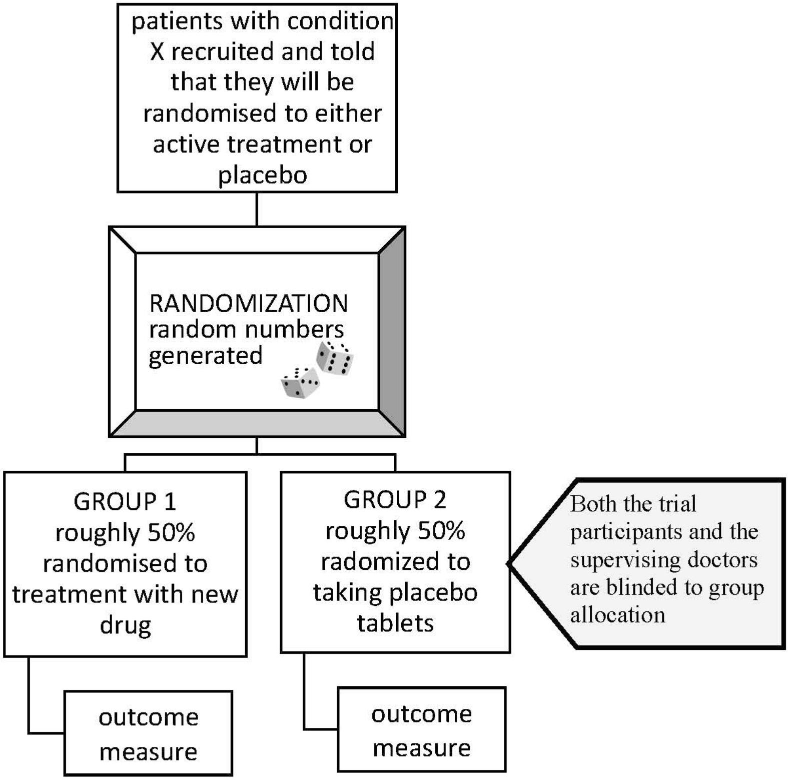


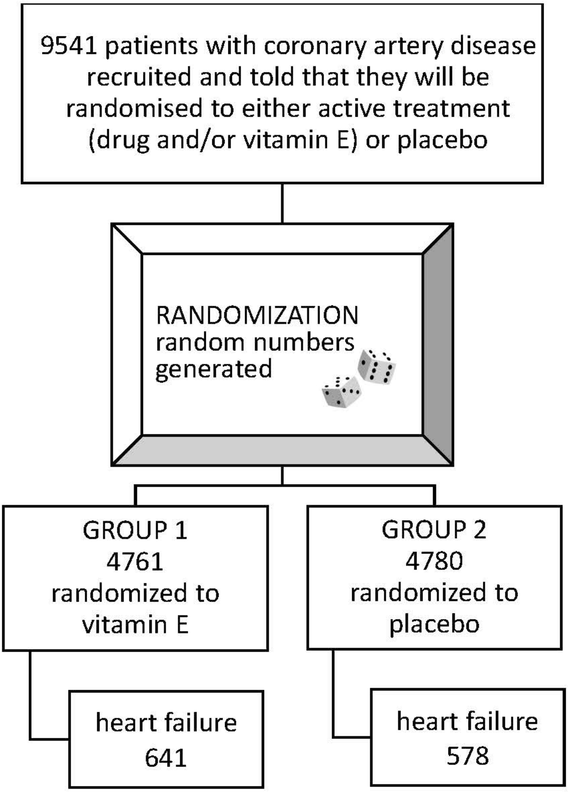
Figure 7. Randomised double-blind placebo-controlled trial



A double-blind trial is a trial of a treatment in which both the participants and the supervising doctors are unaware which participants are on the active intervention (drug or other therapy such as a nutritional supplement) and which are on placebo tablets. The coded key to randomization and allocation is kept by an independent authority and this is often a senior hospital pharmacist. At the end of the trial, the independent authority will break the code and one of the supervising doctors or a scientist involved in the research will be able to analyse the results of the trial.

This approach to research is the basis for "evidence-based medicine" (EBM) drug trials but various authorities in the world of nutrition science have queried its relevance to "evidence-based nutrition" (EBN). A large body of

Figure 8. HOPE trial showed an increase in heart disease with vitamin E



biochemical and epidemiological research has shown links between dietary factors and death from cancers and cardiovascular disease including a protective effect from high dietary intake of vitamin E. However, the HOPE trial a large double-blind randomised-control trial was reported in 2005 that showed the opposite effect (Figure 8). This result was unexpected and difficult to explain. Then the CARET trial in 2017 reported similar adverse results for vitamin A and betacarotene (a vitamin A precursor) in patients at risk of lung cancer. In both cases, the adverse events were seen in patients with moderately advanced disease and I believe this is very significant. A leading theory is that although both vitamin E and A can have a beneficial effect by neutralising small unstable molecules called “free radicals” that cause disease they can become overwhelmed by free radicals in the