

Bishop Berkeley and the Freireich experimental hypothesis

BY CHRIS POTTER

Our resident reporter at large tells us about two of his heroes, both of whom have quite clear merits and foibles.

My patients just keep on getting better. You may well point out that under the care of a clinician of such great wisdom and proficiency, this can hardly come as a surprise but unfortunately they seem to be getting better even before they have had the opportunity to access my unsurpassed clinical acumen. With the delay to see me in clinic currently sitting stubbornly at around a year despite my Herculean efforts, it remains the case that a sizeable minority of my new referrals have spontaneously (if somewhat perversely) improved long before they find themselves in the hallowed cloisters of Buckinghamshire Health Trust.

Before I set out to explain this somewhat irritating phenomenon, please indulge me as I first introduce you to a personal hero of mine, George Berkeley (1685–1753). To say he was a man of contrasts would perhaps be an understatement. For a start, he spent much of his life as an Anglican Bishop in an Irish diocese which, to this day, remains staunchly and profoundly Catholic in faith and custom. Possibly the finest mind of his generation and the great founder of the British philosophical schools of empiricism and subjective idealism, he expended much of his intellectual energy on polemically attacking John Locke and Isaac Newton (with about as much success as his efforts to convert rural Ireland to Protestantism). A profound Christian apologist and man of great wisdom and generosity, he proceeded to undergo an ill-judged midlife crisis which led him to up sticks and set up a plantation in Rhode Island. In what appears to have been a fit of absent-mindedness, he thus became a significant slave-owner, which has led to all manner of problems for his later admirers, myself included.

Trinity College, Dublin (whose gates he first entered at the age of 14) quietly dropped the Berkeley Medal in 2012, which it had previously awarded annually



“Berkeley became famous above all else for his enthusiastic promotion of a great life-saving panacea: tar water”

Figure 1: George Berkeley, busy failing to eradicate Catholicism from rural Ireland. Creative Commons 0: National Portrait Gallery, Smithsonian Institution. <https://npg.si.edu/object/npg.NPG.89.25>

since 1752 for the best performance in Greek translation (confusingly Berkeley himself was a lecturer in Hebrew). However, University College Berkeley – that hotbed of radicalism, activism and deranged lunacy on the West Coast – has not yet seen fit to rename itself and may well remain gloriously unaware of the chequered history of their illustrious benefactor.

During his lifetime, however, Berkeley became famous above all else for his enthusiastic promotion of a great life-saving panacea: tar water. In his 1744 work, *Siris*, he described how drinking the supernatant of a water-soaked barrel of pine tar could cure dysentery, phthisis and plague [1]. In one passage, he gushingly describes how in 1741 alone he successfully treated no less than 25 cases of fever in his own family. Call me cynical, but I’m not altogether convinced.

Time to introduce another hero of mine to shed some light on all this: the original platonic ideal of the difficult colleague, Dr Emil J Freireich (1927–2021). Born in extreme poverty to a Jewish immigrant family at the depths of the Great Depression, his father took his own life when Emil was just two. This left him in the care of a disinterested mother and a positively hostile stepfather. This terrible childhood of adversity and misery gave Freireich a resilience and near-indifference to suffering that were to mark his life’s work.

At the start of his career in haematology, acute lymphoblastic leukaemia in childhood killed 90% within six weeks of diagnosis, usually from unrelenting mucosal haemorrhage. The wards he first attended in Chicago were indescribable charnel-houses of sobbing parents and

exsanguinating infants. Amidst this misery, Freireich was somehow able to maintain his composure and detachment. Showing immense stoicism, he addressed the clinical problems dispassionately and, through a series of breakthroughs of great brilliance and clarity, he eventually gained fame as ‘the man who cured childhood leukaemia’.

Colleagues found him impossibly irascible and combative, and he was sacked on no less than seven occasions from some of the most prestigious haematology departments in the USA. His people skills were negligible and I, for one, would have loved to appraise him for the joy of seeing his personal feedback on his colleague 360. Trainees were rightly in awe of him, and his superiors at the National Cancer Institute barely tolerated his outbursts. But he concentrated all his efforts on saving his patients and ignored any social pleasantries in his single-minded efforts. And he got results. Boy, did he get results.

Away from haematology, his fertile mind came up with an intriguing thought experiment in the early 1970s, which he modestly named the Freireich experimental plan [2]. He hoped to explain how ineffective treatments could appear highly clinically useful when applied under certain circumstances. First one must choose a safe, benign treatment with no adverse effects, perhaps vit B12 injections, homeopathic remedies, Betahistine or even tar water. Bear in mind that the hallmark of just about every highly effective therapy, from insulin to imatinib, is a very low therapeutic index and a host of adverse reactions.

One then chooses a chronic condition with a variable and fluctuating clinical course. A high-risk strategy would be to treat rapidly fatal conditions on the basis that the patient would be unlikely to complain once nature had taken its course and you could explain to the grieving relatives that your efforts were too little too late. However, in most chronic conditions, one expects to have good days and bad days, good weeks and bad weeks (Figure 2). It is of course important to realise that the patient will tend to seek medical help in the trough of feeling much worse than usual. In these circumstances,

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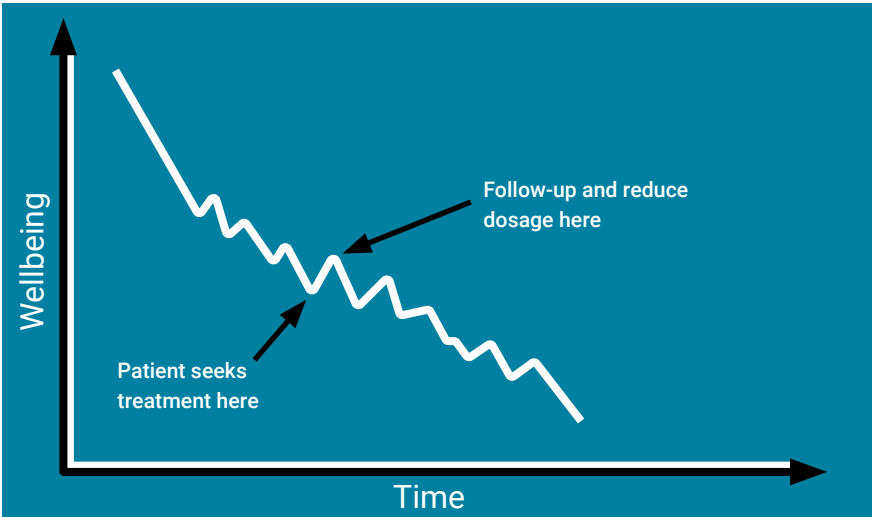


Figure 2: The relapsing remitting pattern of a chronic disease.

it is imperative to see the patient as soon as possible as the symptoms are generally about to regress towards their mean and it is essential to be able to take credit before any improvement occurs by applying one’s ineffective remedy. If the symptoms do not improve but plateau, one can still claim credit for arresting the decline, but an increase in the dose of the (expensive) remedy may be needed. In the unlikely event the patient continues to decline, warn the patient that they may have come too late for effective treatment whilst hiking the dose, and the fees, for treatment.

Follow-up should be frequent and regular. Generally the patient will have improved (by regression) and now it is time to reduce the dose of the therapy. If improvement continues, congratulate yourself for providing a long-term cure and collect your fees. If the improvement plateaus, keep the dosage high and arrange further follow-up. If the patient has deteriorated once again, it only goes to prove that the remedy was highly effective as the reduction in dosage has led to a relapse, so ramp up the dosage once more, arrange more follow-up and hike the fees further. In this way, the random fluctuation of the disease process and regressions to the mean drive the alterations in drug dosage, whereas to the poor patient it will seem the causality is reversed, with changes in the treatment leading to cycles of improvement and deterioration.

Ask yourself which is more likely: that an Anglican Bishop accidentally stumbled across an effective cure for all manner of infectious disease in the mid-18th century or a combination of natural fluctuation in a variety of disease processes combined with regression to the mean gave him the illusion of efficacy via a series of cognitive biases.

Despite our best efforts, the world remains a messy place. Diseases take unpredictable courses, magic bullets are rare, saintly philosophical geniuses make basic cognitive errors and are indifferent to fundamental human rights, and the most awkward of colleagues with very few apparent redeeming features sometimes sees much further and clearer than all of us.

References

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