

A sick well

ESSAY

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According to the dictionary, a 'well' can be a wave (from 'wella' in Old High German), a spring of water, a fountain fed by a spring, or an enclosed space in the bottom of a room, building or ship. In this context, the word is conceptualised in a concrete sense as well as symbolically and metaphorically, and is associated with medical history, the theory of science and social policy. A deep well can be the source of life, growth and health – but also illness, misery and death.



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The North American paediatrician Nadine Burke Harris has written a book entitled *The Deepest Well* (1). The subtitle *Healing the Long-Term Effects of Childhood Adversity* suggests that the author uses the word 'well' to mean a 'source of illness and misery'. Painful and challenging childhood experiences are exactly the type of source or well that health problems can stem from, as has been shown in broad-based research.

In the spirit of the essay, I will now take the reader on a journey. It will touch on aspects that can be regarded as professional viewpoints as well as aspects that allow a synopsis of or insight to this knowledge which has been created over the past three decades. The journey, in a sense, tells the story of my own journey of academic formation in an expanding field of knowledge to which I have also contributed. The journey starts in London and ends in San Francisco, where Nadine Burke Harris now lives and works.

The name John Snow is associated with a fundamental realisation in the field of medicine that heralded the end of a theoretical framework, a paradigm, a professional belief, an episteme. Many doctors will be familiar with Snow's work: he obtained empirical evidence that a well in London was the source of a terrible epidemic and mass deaths. In 1854, his insistence on shutting down a well which supplied the water for an entire neighbourhood was considered insane. Snow did not share the majority's belief that disease was airborne, claiming instead that the cholera outbreak in a central part of London was due to contamination of the drinking water from a street pump. When the handle of the pump was removed, the epidemic abated and the death toll sank. Like the medical pioneers Lister and Semmelweiss, and others since, Snow had done something special: he had investigated a public health problem from a different perspective to everyone else, outside the contemporary authoritative and accepted framework of understanding.

Applying a different theory or perspective from those traditionally used to confirm what is taken for granted, is known in science as 'adopting a critical position', and is essential to the world of academia. To paraphrase social psychologist Tor-Johan Ekeland, academics are actually paid to be critical. The critical approach is often triggered when clarity is lacking, when the logic is flawed, or where there are obvious paradoxes. In an epistemological perspective, such paradoxes take the form of data that requires a different framework of interpretation.

Unknown relationship

The journey continues from our English colleague Snow to our North American colleague Vincent J. Felitti, a specialist in internal diseases and professor at the University of California San Diego. In the mid-1980s, Felitti was pondering a paradox in which the most successful participants in a weight-loss programme at his preventive medicine department did not attend the agreed follow-up. His musings threw up the not entirely academic question of 'What the hell is going on here?' (Felitti, personal message). He took the slightly unusual decision to invite only these individuals to an open conversation about their reasons for abandoning a support initiative that they themselves had originally requested.

The back story to the participants' weight gain was discussed in these one-to-one meetings. The more stories Felitti heard, the clearer it became to him that these people had endured too much, in a biographical sense. Maltreatment during childhood and adolescence emerged as a clear common denominator and source of the problem. Felitti realised that he had to re-examine this anecdotal material empirically. Along with the cardiologist and epidemiologist Robert Anda, he initiated a study in 1993 into possible links between adversity in childhood/adolescence and poor health in adulthood.

The results were published in the autumn of 1998 (2). The study was the first in the world to show that abuse, maltreatment, neglect and growing up in a violent, chaotic and dysfunctional family were associated with a high probability of the main risk factors for the most common causes of death among adults in the USA today, in addition to problems with interpersonal relationships, working life and substance abuse (2). The findings revealed for the first time that all the serious somatic diseases in the adult population had a dose-response relationship with the degree of adversity a person had experienced early in life. The Adverse Childhood Experience Study (ACE Study) represented a new way of examining previously unrecognised or underestimated sources of illness. The findings indicated a deep well in terms of poor public health.

From that to how

While empirical research was being conducted in San Diego to show *that* childhood adversity was associated with health problems in adulthood, several research groups were working elsewhere to show *how* this was the case. How could the finding that a subjective mental phenomenon or experience could be a predictor of an objectively demonstrable somatic illness be explained scientifically? The question was often formulated as follows: 'How does adversity get under the skin?' (3).



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This leads us to the University of Ohio, Cincinnati, where around the same time, the endocrinologists Ronald Glaser and Janice Kiecolt-Glaser and their colleagues began to explore the impact of stress on the immune system. They demonstrated that various forms of short-term stress (taking an exam) and long-term stress (caring for a loved one with Alzheimer's disease) reduced the expected immune response – measurable amounts of antibodies – to regular doses of known vaccines in healthy volunteers. The conclusion was that major stress weakens the cellular immunity against infections (4, 5). This prompted the question of whether the hormonal aspects of the immune system were also affected. This was subsequently demonstrated in a number of studies which confirmed that long-term overload was associated with inflammation (6).

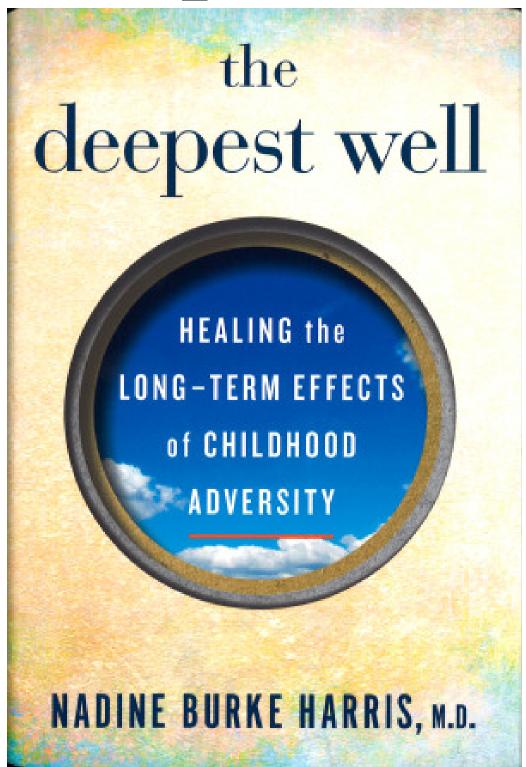
In New York, a group of researchers affiliated with the neuroendocrinologist Bruce McEwen were developing a model that could embrace the growing empirical evidence of the relationship between long-term stress and disorders of the central nervous system, hormone system and immune system. In autumn 1998, when Felitti and Anda published the findings of the study, Bruce McEwen wrote a ground-breaking article in the *New England Journal of Medicine* (7). In the article, he promulgated the allostatic overload model, which explained how high levels of prolonged activity in the so-called stress axis from the hypothalamus via the pituitary gland to the adrenal cortex interferes with the regulation of all vital, life-preserving bodily functions (8). This was the pathophysiological basis for understanding the phenomenon of multimorbidity (9), as well as an inroad to understanding the proven social gradients of disease in any population – the pathophysiology of social disadvantage (10).

On the other side of the country, in San Francisco, the Nobel laureate in cellular biology Elizabeth Blackburn was working with the psychologist Elissa Epel to show how caring for a chronically sick child over a long period of time affected healthy young mothers by harming their telomeres (located at the tip of chromosomes). Cell ageing accelerates, which represents a central attack on the health of the mothers (11).

A new map emerges

The map of the journey so far and its numerous points of reflection shows a diverse terrain with various specialist fields and multiple disciplines. The terrain includes classical epidemiology, clinical fields such as psychology and neurology, basic medical sciences such as immunology, endocrinology, cellular biology, genetics – including the emerging area of epigenetics – and neuroradiology, consciousness research and much more. The specialist fields have added pieces of the puzzle to an increasingly detailed and sharper image that reflected the effect of biography on the human body's biology (12). However, despite collaboration across the fields steadily increasing due to the growing insight into the historically conditioned arbitrary nature of the disciplinary divisions, these pieces of the puzzle did not just readily come together. The divisions started to disintegrate, and it was gradually recognised

that mental and physical trauma could trigger the same bodily phenomena: chronic pain, impaired immunological response to microbes and abnormal cells, increased inflammatory activity, disturbances in glucose, lipid and mineral levels, disturbances in various autonomic processes with increased resting heart rate, blood pressure and muscle tension, and poor sleep and digestion. This represented a challenge to biomedicine's traditional understanding of causality (13).



Book: Nadine Burke Harris. The Deepest Well. Healing the Long-term Effects of Childhood Adversity. Boston: Houghton Mifflin Harcourt, 2018.

Putting the pieces together and seeing them gradually shape a radically new map that is actually more closely aligned with the clinical reality of the medical profession, especially in general practice, can become a passion. I can attest to this. I know the joy and relief when another pixel fits perfectly into a 'white spot' on the map where new findings were bound to emerge sooner or later, and where this supports an understanding of long-term adversity as a source of illness.

'Exactly' is the word that springs to mind at a moment like this. The research group of Martin Teicher, an associate professor of psychiatry at Harvard University, Boston, invoked one such 'exactly' situation when it presented a review of all studies that had been conducted on the relationship between childhood adversity and changes in brain structures, functions and network architecture (14). Overall, these studies document how painful and difficult experiences are literally inscribed in the body's physiology in a way that is closely linked to when and how the adversity occurred. Teicher's research group believes the findings require radical reflection: can psychiatric epidemiology have interpreted the proven structural and functional abnormalities – the *effect* of integrity violations – as if they were the *cause* of mental illness?

The journey to knowledge-producing places also takes us to New Zealand and the researchers behind the Dunedin Study, a prospective follow-up study of a representative sample of newborn babies from the 1972/73 cohort (15). Followup studies were conducted on the cohort at ages 3, 5, 7, 9, 11, 15, 18, 21, 26, 32 and 38, with 95 % of the sample still in the follow-up group after 40 years. At the start of the study and in the three-year follow-up, the researchers defined the term 'childhood risk', characterised by childhood socioeconomic deprivation, exposure to maltreatment, low IQ and poor self-control. The findings for the three-year-olds were shown to predict with low to moderate accuracy which of these children would end up in various high-risk groups as adults. When combined, the four criteria for childhood risk accurately predicted which cohort members would be in a 'multiple high-cost group' as adults. A quarter of the cohort accounted for 66 % of the cohort's total welfare benefits as adults. This quarter smoked 54 % of the cohort's cigarettes, accounted for 40 % of the excess weight kilograms, 57 % of hospital admissions, used 78 % of all prescriptions and were convicted of 81 % of all criminal offences. Thirty per cent of the cohort accounted for almost 100 % of the welfare benefits received by the cohort.

Nadine Burke Harris

With these figures added to the collection, the journey ends in San Francisco with Nadine Burke Harris, who gathers knowledge pixels with the same passion as myself. Her point of departure was also clinical experience, in her case from meetings with children in a practice in the deprived district of Bayview-Hunters Point. She was disconsolate that the terrain, which was her professional stomping ground, did not match the map – the textbooks she had studied for many years. When she discovered the publications of Felitti et al. (2), she knew she had glimpsed a deep source of human misery and illness. Using this study

as a basis, she began to seek the knowledge that would take her from knowing *that* it was so to understanding *how* it was so. Deeper understandings can lead to more appropriate treatment.

Nadine Burke Harris' own story of this journey of realisation begins with a boy named Diego, who was small for his age, but otherwise seemed healthy, well-adjusted and full of life, and with Kayla, who had asthma attacks that were difficult to control (1). Harris became curious when Diego's mother said that her son stopped growing after he was sexually abused by a babysitter. And when Kayla's mother, on the question of whether the attacks followed a pattern, replied: 'Well, her asthma does seem to get worse whenever her dad punches a hole in the wall. Do you think that could be related?', she saw a connection.

Harris writes prose in a free and engaging style about the inspiration she felt after finding a map (theoretical framework) that suited her terrain (clinical practice among socioeconomically deprived families). The book begins with a story about a 43-year-old man who suffers a stroke, despite having no single *known* risk factor. The book ends with the revelation that this man is the author's brother Evan, who, like the author herself and her brother Louis, grew up with a mother with diagnosed schizophrenia. Louis was diagnosed with schizophrenia when he was 17 years old. At the age of 19, he just disappeared one day.

Harris writes about how her own biography has influenced her choices as an adult: 'Louis is what brought me to Bayview-Hunters Point.'

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