

Cultivated cure, regenerated affliction

Encounters with ALS and stem cell regeneration in India

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Abstract

In this think piece, I interrogate the notion of cure in order to address the idea of disease. My intention is to show how emerging biotechnological modalities that cultivate an idea of ‘cure as regeneration’ dislocate expert knowledge, descriptions of disease, and its representation into contested new terrains. In approaching disease from the vantage point of the ‘cultivated cure’ I seek to trouble our commonsense view of afflictions. Drawing on ethnographic data from a longitudinal project engaged in mapping stem cell technologies in India, I conceptualize how ‘cure as regeneration’ reanimates the figures of disease and medical knowledge. I take up Veena Das’s challenging query: is it necessary to define terms – illness, disease, diagnosis, health – that defy neat characterization?

Keywords

affliction, cure, ALS, stem cells, India

Diseases are new ways of life.

– Georges Canguilhem, *The Normal and the Pathological*

Introduction

Veena Das (2015) encourages scholars to view everyday life as a site for cultivating cures for gestating afflictions. This think piece is inspired by her pertinent query: ‘Is it necessary to define those terms – illness, disease, diagnosis, health – through which we intuitively come to know the disturbances in our world but that defy any neat characterizations’ (Das 2015, 212)? As she rightly argues, the issue at stake is not merely that of discerning meaning but also of ‘trying to understand what the *being* of this entity (illness, disease) is that seems to have such a restless relation to one’s own experience and such a need to find authorization of “its” reality’ (Das 2015, 213). Das’s ethnography skirts around a preoccupation with categorical clarity and instead arrives at a range of questions that arise in relation to the shifting lines of illness and health in low-income neighbourhoods. I wish to suggest that the chronic and progressively pathological affliction may be a site for witnessing the anatomy of a cultured and cultivated cure from within the emergent field of regenerative medicine. A cure is ‘cultivated’ in the sense that it is the enmeshment of: 1) the constant refinement of interventions tailored to a patient, 2) the culturing and tending to stem cells as a therapeutic agent, and 3) the ways in which the patient responds to disease through a work on him or herself. How might we see a progressive and aggressive affliction as paradoxically regenerative, in the face of curative operations that end up maintaining a tenuous truce, a dormant zone, that can be imagined as health? This fleeting ‘health’, wedged precariously between a cultivated cure and a regenerating affliction, offers fascinating insights into the emerging world of stem cell therapeutics.

But what is a cure? It is, I argue, the restoration of a dormant state. To cure is to cultivate and return (the body) to a normative state of dormancy known as ‘health’. It is a dormant space where illness is forgotten and paradoxically cultivated for further curative operations. It is a deep sleep in which illness is a bad dream. An affliction in this respect is an awakening from a dormant state. A chronic affliction can be likened to uninterrupted wakefulness, a state of chronic sleep deprivation. This wakefulness (re)activates the dormant circuit of pain and suffering.

Disease, as Georges Canguilhem (1998, 40–41) reminds us, is a generalized reaction designed to bring about a cure; the organism develops a disease to get well. This struggle in the ‘natural’ order creates conditions for tolerating infractions of established norms, and for establishing new norms under new conditions scripted by afflictions. In other words, afflictions rouse pathology to life and life to a state of pathology. In this respect a cultivated

cure is a struggle to normalize pathology to a point of dormancy. I visualize the notion of dormancy as the two faces of Janus: dormancy is both ‘health’ and silent affliction. These operations seldom re-establish the norm but instead merely ‘cure’ pathology to the point of establishing a new normal (Canguilhem 1998). The notion of cure in this respect is also doubly articulate. It relieves or resolves an affliction – its cause, symptom, chronic manifestation – or it preserves or hardens (like cured food or substance) a state of pathology. In each instance a cured affliction is cultivated and prone to mutation. In the dormant state, moments when seemingly nothing happens, destinies of pathologies and their intended cures are relentlessly cultured and shaped. A state of dormancy, or ‘health’ in this respect, is a mirage; following Canguilhem (1998) one can argue that an affliction can ‘play its tricks’ at the subterranean (tissue) level: (undetected) sickness can exist without a sick person.

The foregoing is the theoretical plotline underscoring the culture and cultivation of emerging embryonic stem cell cures for some of the worst known chronic and progressive afflictions. In this essay I take the therapeutic journey of an amyotrophic lateral sclerosis (ALS) patient as a route into the undulating typography of afflictions and human embryonic stem cell ‘cures’. I am not attempting to explain away the anatomy of an affliction via glib definitional fiat but rather taking a tentative step into ‘ethnographic reality’, co-conjured with the afflicted, to decipher how zones of dormancy and the affliction’s eventual activation produce shifting manifestations and meanings of disease and health that often defy being captured by language.

Material and methods

The ethnographic focus is a small clinical facility in New Delhi. Since 2002, I have followed the culture, cultivation, and clinical application of human embryonic stem cells (hESC) at this facility. The clinic is a small player in the high-stakes world of regenerative medicine. It is seen as a rank outlier and is often criticized for having moved too quickly ‘from bench to bedside’ without passing certain critical scientific milestones that have become accepted as the gold standard within the Euro-American landscape of science and biomedicine. I have described the politics of name-calling and ‘subalternity’ involving the clinic and how the clinic has addressed these long-standing criticisms elsewhere (Bharadwaj 2015); here I delve into one longitudinal conversation with an ALS patient I have been following since 2013. The larger research project in which this think piece is embedded examines the emergence of stem cell technologies within the scientific, ethical, and regulatory landscapes in India (European Research Council, grant number 313769). Interactions with the growing number of Indians and foreigners seeking treatment shed light on the contingent nature of healing and agency, and the wider reaction to hESC-based therapies.

Methodologically I grapple with the question of whether ethnography is meant to illustrate a theoretical argument or whether theory might be built into ethnography itself (Das 2015, 15). I hope that as the reader's immersion in the life of the ALS-afflicted patient featured in this think piece deepens, theory will begin to embed itself in the structure of a life rattled and threatened. The conversation I report is not so much in pursuit of building a theodicy, to make sense of an afflicted life, but rather to reclaim a contracting zone of health in the face of a rousing affliction.

'Cured' affliction

ALS is a form of motor neuron disease. It attacks the nerve cells responsible for voluntary muscle actions, leading to the progressive weakening of muscles and eventual death. ALS can be inherited (in 10 percent of cases) or manifest randomly. The causes can range from genetic mutation to an imbalance of the chemical messenger glutamate to an autoimmune response that can cause the immune system to attack functioning nerve cells and protein accumulation within nerve cells, resulting in nerve-cell death. The prevalence of ALS in the United States is 32 per 100,000; because most epidemiological research on ALS is confined to the United States and Europe, it is at present difficult to provide global incidence and prevalence rates (Chió et al. 2013). At present no known and credible 'cure' for ALS exists. The drug riluzole is the only approved treatment believed to slow progression of the disease, and it is usually prescribed from the point of diagnosis. However, even in the best-case scenario, riluzole can help control some symptoms and extend one's life only by three months. At \$2,035 per month, the drug is extremely expensive.

Recently ALS attracted global attention through the Ice Bucket Challenge, a campaign to raise awareness of the disease by encouraging people to videotape themselves pouring a bucket of ice water over their heads, and to challenge acquaintances and friends to do the same, with some participants donating to ALS research. However, despite the growing awareness of ALS around the globe, the condition is relatively unknown in India. It is therefore no surprise that my only encounters with the condition occurred in the context of hESC treatments at the New Delhi facility, where globally mobile treatment seekers, on their peripatetic quest for hESC 'cultivated cures', routinely came.

I met Warner (pseudonym) in New Delhi when he first visited the clinic director's consultation room in May 2013. He was trembling, and his hands and arms were shaking with rapid fasciculations. The quivering skin and spasmodic activity were unremitting, and his speech was slow and frequently inaudible. Warner had been diagnosed with ALS in early 2013 and given fewer than three months to live. A qualified surgeon who understood biomedical prognoses, he looked for alternatives to fight the disease's rapid progression.

One of his colleagues in Germany, who had seen some of his patients undergo successful stem cell treatments in the New Delhi clinical facility, suggested he try hESC treatment.

Warner had led an active life and had been a formidable athlete, running a full marathon in 2005 and several half marathons until 2009, when he noticed muscular fasciculations inexorably rising from his legs to the rest of his body and down his arms. He consulted eminent doctors, including professors of medicine (some of whom were his colleagues), and was put on hormonal therapy involving cortisone. Magnesium and calcium prescriptions quickly followed. However, his body continued to tremble. He underwent a battery of tests, including an electromyogram conduction test, and nothing untoward was discovered. Similarly, no antibodies were discovered, and the specialist surmised it could not be ALS but only benign muscular fasciculations and cramps. Warner researched his condition on the internet extensively but still couldn't piece together the mysterious symptoms that inexplicably waxed and waned. He soon readjusted to 'a new normal' and began to shape his life around this constant annoyance. However, when he returned to his active life and running, the cramps became more persistent. By the middle of 2012, his strength had rapidly deteriorated, and he was unable to lift his foot.

In mid-2012, however, Warner continued to push himself in the face of his deteriorating condition. He noticed the changes but could do nothing except moderate his running around his fatigue. He could only run seven to ten kilometres, a daunting task for a physically 'fit' person, but a huge setback for an enthusiastic long-distance runner. To make matters worse, his breathing had rapidly deteriorated and become laboured. In October 2012, his cramps became so severe he could not sleep at night. Desperate to find a resolution, he began to reach out to specialists for an expert referral but received only a prescription for sleeping pills.

By 2013 Warner's muscles had significantly weakened, and he began to lose weight. Despite increasing his calorie intake, his weight and muscle strength were in free fall. In May 2013 he consulted a top neurologist at one of Berlin's leading hospitals and was devastated to receive a firm diagnosis of chronic ALS. He was told that his ALS was so serious 'it must be carried on the shoulders of many doctors'. Second and third opinions only corroborated the diagnosis of 'motor neuron disease sub-form ALS, sub-form peripheral muscle atrophy'.

It was as if the horrific affliction that had lain undetected deep within Warner's folding tissue while 'healthy' Warner ran marathons had suddenly roused from its dormant slumber to regenerate itself as pathology demanding a cultivated cure. The destinies of cures and afflictions are inextricably linked. Even in the best-case scenario, where an affliction is pushed back into a state of hibernation, normality and 'health' reappear truncated. In

Warner's case, it was clear his strength could only return by putting the affliction to sleep. The cultivated cure he had embraced above other cures (such as riluzole, occasionally extending life by three months) could work to either return the advancing ALS to a state of dormancy or 'cure' or 'harden' it still further.

Warner is a general surgeon but has a fair amount of neurology in his training and surgical experience. He understood exactly what he was up against and was networking relentlessly to figure out an 'alternative' to mainstream cures that paradoxically only 'hardened' the affliction. It was through the course of actively researching an alternative that a colleague mentioned a doctor in Bavaria, who had patients return from India after hESC treatments. However, the process of establishing contact with the doctor was not easy: their phone calls remained unanswered, and automated messages announced the clinic wasn't accepting new patients. It was as if Warner's life had suddenly hit the 'complication' stage in the Labovian narrative structure (Labov 1972). The persistent Warner, however, sent urgent emails and heard from the doctor eventually. After running several baseline tests, she concluded that hESC treatment in India was their only option.

Warner arrived in New Delhi looking forward to the treatment. Unlike many other Germans and Americans I had spoken to, he displayed no dismay or culture shock upon arrival but only reiterated his wish to get his life back, a 'healthy' life contained in a web of kinship and bonds of affect. In this tightly knit unit, his wife, daughter, and in-laws featured prominently, people who loved him and cared for him. Warner's wife and her father, with whom he had a strong bond, accompanied him on the trip. Warner was steadfast in his resolve to fight the advancing ALS and had prepared himself for the eventuality that, if his pursuit of a cure failed, he would not be afraid of his end. He often remarked to me and his wife that he knew how people with life-threatening diseases coped and that he had, in consultation with his wife and supportive family, come to the decision he would do everything in his power to resist a future that would reduce him to an entity strapped to a ventilator. If the treatment failed, their plan was to go to Switzerland to bring his struggle to a peaceful end via assisted suicide.

Warner was finally ensconced in his small room at the clinic and began looking forward to the stem cell insertions. 'I have no idea what to expect', he said, a frequent statement of his. Warner firmly believed he had nothing to lose. He was looking for incremental progress, and his first priority was to stabilize his breathing. Warner didn't have much time to relax and adjust to his new environment, however, as he was almost immediately put through a series of diagnostic tests and exams. He felt utterly exhausted as the clinicians swung into action. The clinic had treated ALS patients, and the clinical director and her team were accustomed to treating patients who were in the late stages of disease and seeking hESC therapy as a last resort. Judging by ALS standards Warner was a difficult case; the clinical team had not seen

such a complicated one before. His intimate understanding of how aggressively ALS progressed helped. Although the pace of tests and protocols left him feeling utterly exhausted and ‘smashed’, from a clinical point of view there was no time to waste due to his rapidly worsening condition, and the team needed to gather as much information as quickly as possible. This was normal protocol in less severe cases, but because Warner’s condition was deteriorating they had to rush through the process to precisely engineer his stem cell protocol.

Around the second day Warner was put on an intravenous stem cell test dose, followed by intramuscular stem cell injections. His body was gradually prepared to respond to the cellular infusion, until finally, on the day of our longest conversation, he received an invasive stem cell-loaded spinal epidural. When I asked if he had experienced any changes since he started getting being treated, he responded, ‘Any changes’, he laughed, and continued: ‘I am the luckiest man, you can see, because this [gesturing toward the floor] was what I was before and now [I am here]’, he lifted his hand to indicate progress. Severe cramps in his body, including his neck, had receded, and he had begun sleeping for hours at a stretch: ‘Last night. . . . I slept two hours – [it was the] first time in two years I slept [uninterrupted for two hours] – and I had no [leg] cramps at all, no, no cramps at all. And, you see, I only got the proper spinal [epidural] today. So, visit me in three or four days and you will see [how many changes]!’

He noted that in the previous two days he had been walking with a stoop, like someone with a severe stomachache. He compared it to walking like ‘an old stick’, bent, then said: ‘but in the morning I walked straight, walked normally, and my body was like a young tree and not an old oak. During the last twelve, fifteen to sixteen hours it changed!’ I responded, ‘It’s dramatically fast. Don’t you think?’ He replied, ‘Yes, yesterday in the morning I was speaking to my wife, and I said yesterday, “I want to die”, and this morning it is like this. I write every day what I feel. I am maintaining a diary’.

Warner’s account was truly heartwarming. It was as if the stem cell cure tranquilized the advancing ALS. And as the aggressive symptoms slumbered Warner could at long last detect a vital new normality, a faint state of ‘health’ that had been dormant. Elsewhere I have documented the strong criticism of hESC stem cell treatment at the clinic (Bharadwaj 2013a, 2013b, 2015). Most striking of these is the suggestion that patients, in their desperate, terminal state, were duped into thinking they were recovering when they were merely experiencing a placebo effect, and thus were victims of quackery. I checked on the placebo issue with Warner. Given his biomedical training, he was uniquely placed to comment on the role of placebo in bringing about such a sudden and dramatic change. He laughed as he responded:

I know, because I am a medical doctor, so I know what a placebo effect is. And I am more critical as a patient and I don't want a placebo effect, I want to be cured. So I was astonished after first, second injection and at night I felt like I [have] never felt before. I have a restless feeling so I couldn't sleep and by morning it's gone and I told them [the clinic staff]. Then I had other problems [cramps and contractions] and had it really bad until last night. And then it was as if someone has switched something [on]. That's no placebo!

In May 2014, exactly a year after his first treatment, I flew to Berlin to meet Warner. We arranged to meet at his home, with its meticulously planted garden that he had nurtured over the years. Warner answered the door and ushered me into the living room, where we spent the afternoon in the company of his wife and in-laws drinking tea and enjoying home-baked cake. Warner updated me on his progress. He was continuing to get stronger and could even work part time. His recovery narrative was interspersed with stories of setbacks, surprising recoveries, growing stamina, and muscular strength. He even maintained a 'peak flow' graph that painstakingly tracked his daily progress through March, April, and May. A little later we all walked two blocks to a neighbourhood restaurant for dinner. The evening was spent talking and laughing as Warner enjoyed his food, without once complaining of exhaustion.

Later that year Warner returned to Delhi for his 'top-up dose', followed by another round of treatment in early 2015. He was initially surprised that the clinic insisted he return for frequent 'top ups', as he thought he would only have to return annually. But the clinic director was clear: the affliction he was countering was aggressive and needed constant stem cell intervention. The cultured embryonic stem cells worked as Warner had expected, and so did ALS, continually regenerating itself to re-establish a new pathological norm. Warner and his wife believe the stem cells allowed them to cheat death. He has lived two years longer than he would have had they allowed ALS to assert its wakeful dominance 'unchallenged'.

Conclusion

Health is caught up in a landscape of possibilities, connections and disconnections, mutations and aberrations. Following a chronic and degenerative disorder, one is reminded that health can be an aberration, a state of pathological silence. Similarly, vigour and vitality can be imagined as pervasions of lethargy, a subcutaneous or hypodermal weariness, lassitudes that can accumulate and saturate cellular structure and erupt to the surface and beyond the dermal frontier. Affliction oozes, expels, and pushes forth from beyond the depths of frail tissue to the topography of the body. It's a loop: outside in (micro-organisms), inside out (genetic), and a dialectic of outside and inside (epigenetic). The map to promised health is ensconced in the anatomical atlas.

Warner's struggle with ALS illustrates the search for defining, identifying, and naming an affliction. His experience captures the moment his 'health' or dormant illness awakened into a rapidly worsening affliction. His struggle to establish the ALS diagnosis and his subsequent search for a cure offer a fleeting glimpse into the conceptions one harbours about what the doctor or expert knows and how that relates to what the patient knows and experiences (Das 2015, 219). In Warner's case, with every stem cell insertion the affliction was seemingly 'cured' to a point of dormancy that began to resemble an imagined state of health. Following Canguilhem (1989), structural conditions for afflictions can lurk in the corporeal depths or produce manifestations that interact with the external environment, which get folded into the intricate latticework of tissue. Stem cell insertions are tantamount to lulling 'cured' or hardened ALS to precipitate another cycle of cellular interpolation. Regenerative medicine shows that a chronic affliction can be 'cured', but we seldom see the precise separation between 'cured' as softening and 'cured' as the hardening of an affliction. We continue to mistake the state of dormancy as health. In this respect Rene Leriche's notion of health as 'life lived in silence of the organs' (quoted in Gutting 1995) cannot be understood as the mere absence of disease but rather as a subcutaneous or peripheral stalking, one that eventually breaks the misleading silence. In this respect, and rather ironically, afflictions remain present in their purported absence.

An affliction is an echo. I suggest that an echo is a memory made tangible. It's not merely a memory of that which has gone before, but rather it is both the tail end of what has occurred and what is not yet over. It's a trace of what is ebbing out of existence and, in so doing, reinforcing both the memory of the event and its actual experience. The structural and environmental conversation continues to build, layer upon layer, the conditions for regenerating afflictions, cultivating cures, and new norms of ever-changing normality. As the extreme case of ALS shows, if there is such a thing as health then it can only be grasped in its absence. Health is a mere attachment to a norm that slides to new normative functioning stability as it interacts with regenerating afflictions. In the final analysis we have to come to terms with the idea that sickness and health are not antithetical but rather that they co-exist. Health and afflictions co-exist, hidden, silent, in deep sleep, only to rouse at a time and site of their choosing.

About the author

Aditya Bharadwaj is a professor at the Graduate Institute of International and Development Studies, Geneva. His principal research interest is in the area of assisted reproductive, genetic, and stem cell biotechnologies and their rapid spread in diverse global locales. In 2013, he was awarded a European Research Council Consolidator Grant to examine the burgeoning rise of stem cell biotechnologies in India. Bharadwaj's work has been published

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