

How Clinician-Scientists Think[†]

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Abstract

Science is a human activity and like all human activities, it has its share of drama and pathos. The scientific product is often an interaction of certain ways of thinking, personality traits, and circumstances. This essay examines these factors and how the melding of that could lead to breakthrough discoveries. It may in some instances, go wrong, or take a morally ambiguous path.

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In 1984, a 29-year-old internal medicine resident named Barry Marshall, was working in the Freemantle Hospital in Perth, Australia, when he became intrigued with the observation made by a colleague, J. Robin Warren. Warren, who was a pathologist in the Royal Perth Hospital, found a large number of a previously unidentified bacterium in the biopsed tissues of patients with gastritis. This, itself, was surprising as the conventional wisdom was that the stomach was sterile – the gastric juice (which is so caustic that it could dissolve iron nails and the enamel of teeth) was assumed to be able to take care of whatever microbes that made their way to the stomach. At that time too, the cause of gastric ulcers was almost universally held to be due to psychological stress – “a disease of tense, nervous persons who live a strenuous and worrisome life” in the words of a contemporaneous and highly regarded gastroenterologist.¹ Flying in the face of these conventions, Marshall hypothesised that these bacterial infections were the cause of gastritis and gastric ulcers.

Marshall first tried to present his theory at the meeting of the Australian Gastroenterology Society. Of the 67 submissions for this meeting, only 8 were rejected and Marshall’s was amongst the eight. Undaunted, he tried and succeeded in presenting his paper in Brussels a few months later before an august audience of infectious disease experts. He was met with disbelief and ridicule – a number thought him to be “mad”. The main problem was that he had problems demonstrating that these organisms caused gastric ulcer despite his success in growing pure cultures of the bacterium which was named *Helicobacteria pylori*. Previous experiments to induce ulcers in rats and pigs were

unsuccessful. In an “act of desperation” and to “close the circle”, he went to his laboratory one day and conducted a human experiment on himself by drinking a draught containing billions of this bacterium – which he called “ulcer bugs”. He subjected himself to 3 endoscopic examinations and biopsies: the first before his fateful downing of the bacterial cocktail, the second a week after (which shown gastritis when there was previously none), and the third that showed resolution of the gastritis after treating himself with bismuth and antibiotics.

His doggedness in pursuing his theory precipitated an avalanche of clinical and epidemiological research – done by him and others – that proved the validity of his theory, the widespread prevalence of this bacterial infection in the gut in many other populations, the subsequent therapeutic trials which showed that gastric ulcers could be cured, and its link to gastric cancer. In 1995, Marshall received the Lasker Award, and in 2005, both Warren and him were awarded the Nobel Prize for Physiology or Medicine.

The historian, Thomas Kuhn, in his 1962 book *The Structure of Scientific Revolutions* described the advance of science as “a series of peaceful interludes punctuated by intellectually violent revolutions”.² The architect of such a “paradigm shift” – a term that was introduced by Kuhn – is often a maverick like Marshall: someone who broke out of the confines of their field, broke with the conventions of the day, courageous enough to stick his neck out, in doing so created “revolutionary science”. Marshall had – in the words of a fellow researcher – “the vision and the precision which is so much needed in science”.¹

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However, there is more to it than vision and precision. Studies have found that productive scientists have a distinctive creative capacity that is a mixture of exceptional cognition and personality, and that they perceive and think differently from less creative people when confronted with the same event.³

Dean K. Simonton, a psychologist from the University of California at Davis, has spent more than 2 decades studying creativity. Creative people, he writes, have “a flat hierarchy of associations” while those with low creativity have a “steep hierarchy of associations”⁴ – meaning for an event or observation, a person with low creativity, that is, steep associative hierarchy would think of one or two associations or responses in a highly predictable and conventional manner; whereas a creative person with a flat associative hierarchy would generate many possible associations and are not bound by preconceptions. Another way of putting it is that creative people have a capacity for divergent thinking which is very flexible and prolific in generating multiple answers or ideas in response to a question in contrast to the convergent thinking of less creative people who would generate one or two responses. Linus Pauling when asked about how one creates scientific theories, replied that one must try to come up with many ideas – then discard the useless ones.

The ability to do this may be due to the way the brains of highly creative people are wired. They are less likely to censor stimuli from both outside their brains and from within their minds – sometimes referred to as an altered “filtering mechanism” which is far more porous and let in ideas and thoughts unfettered. They would, therefore, be far more open to ideas and experiences.⁵

These qualities of openness and flexibility of thinking are related to, and augment each other. By being receptive to different perspectives and ideas, they are able to have at their disposal a wide repertoire of ideas and problem-solving strategies, the combination of which may lead to novel ideas or useful solutions.⁶

To possess these qualities of a creative mind is not enough to achieve anything significant. It requires expertise in the domain that the person operates in.⁷ The domain is the area of knowledge, that is the body of facts, concepts and techniques that define that particular discipline. Within that domain and possibly in other domains as well, creative scientists also tend to have a large number of projects that may be independent of each other, which nonetheless often results in “cross-talk” among the projects and among the experts in and outside the field – a process which may lead to unexpected solutions or insights.⁴

In the history of science too, serendipity is often depicted as the midwife to many momentous discoveries.^{8,9} Although chance may play a part, an unexpected event or finding,

however, would only lead to a discovery in the presence of a creative mind – in Louis Pasteur’s words “chance favors only the prepared mind” as was the case of Dr Judith Swain. In 1985, Dr Judith Swain was on sabbatical at the Harvard Medical School. She had embarked on a study with Dr Philip Leder to study the effect of a cancer gene, c-myc, in mouse embryos. Contrary to expectation that the gene is always expressed among the mice, the expression of the gene in heart muscle seems rather random. However, hoping to learn something more, Swain pored over the data again, and described this in an interview with the New York Times¹⁰: “I remember the moment... I was sitting at my desk one evening and I realised that every time the gene was inherited from the male, it was expressed and every time the gene was inherited from the female it wasn’t.” That insight led to the discovery of the first in vivo model of genetic imprinting.¹¹

She was able to pick on subtle patterns that others would have missed – what Albert Einstein described as a *feeling for the order lying behind the appearance*. Intuition is often evoked in these instances and intuition is often held to be something mysterious and vague. It is, however, more likely a cognitive skill that is a combination of a creative mind, knowledge and current involvement in different lines of inquiries that enable these flashes of insight when presented with either little information or a novel situation.

There is a famous phrase in the field of personality and psychology: *Personality is something and does something*.¹² A scientific achievement is not only a product of a creative mind but also of certain personality traits. The most eminent and creative scientists also tend to be more driven, ambitious, achievement-oriented, and far more competitive than their less eminent peers as typified by Judith Swain’s credo – “It’s not, ‘Can I compete? It’s, ‘Can I be the best?’”

One of the criteria of creativity is that it must not only be novel but useful. The usefulness and potential impact of a new idea may not be evident to most people as it is often presented ahead of their time. Therefore, creative people must also have the ability – which requires a certain empathy coupled with confidence – to present their ideas in a socially acceptable manner so that others can understand, appreciate and accept. In this aspect, the tragic story of Ignac Semmelweis as recounted by Sherwin Nuland in his book, *Doctors*, is a cautionary tale.¹³ In 1847, when he was a 28-year-old obstetrician in a hospital in Vienna, Semmelweis made a momentous observation. He saw that the number of maternal deaths from childbed fever in a ward where deliveries were done by doctors and medical students were almost 10 times than of another ward where the deliveries were done by midwives. The rate of maternal death among women who delivered at home was even lower. He made the connection that the cause was due to the

transfer of some purulent material carried on the hands of the doctors – who dissected cadavers – to the mothers on whom they did vaginal examinations with their unwashed hands. Semmelweis made the doctors working in his wards wash their hands, and the rate of maternal deaths fell dramatically. However, he failed miserably to convince other doctors of his theory and its clinical impact. It was not because he presented an unpalatable and inconvenient truth that these deaths were caused by the very hands that were supposed to heal although that would have created some resistance. He failed largely because of some other personal failings. He never did the animal experiments that might have helped him convince his peers. He did not publish his results. He interpreted every criticism as a personal attack and felt persecuted by the medical establishment. He did finally publish his findings – and his frustration – in a rambling and vituperative book *The Etiology, The Concept, and the Prevention of Puerperal Fever*. The first part was a wordy description of his theory, and he devoted the second half to attacking his critics and detractors. What was clear in that book was the indication that he was turning mentally unwell. Following the publication of his book, he developed bouts of depression, impaired memory and bizarre behaviour. He had to be subsequently committed to a private asylum.

Therein lies the potential darker side of creativity: the qualities that lead to creativity may also lead to a tendency towards psychopathology.^{14–16} Certain studies on creative people showed abnormally high scores on psychoticism in their personality tests.^{17,18} Radical, unconventional, asocial, or even antisocial behaviours are probably more common among artists than scientists, but these traits are nonetheless elevated in creative scientists relative to norms.^{19–23}

Nancy Andreasen, a psychiatrist and physician-scientist, drew the parallel between the creative state of mind – where associations in the brain are flying freely and in a rather disorganised fashion prior to organising – and the psychotic state of mania or schizophrenia.⁵ The other mechanism is the altered “filtering mechanism” which allows a flood of stimuli which in a creative person is coupled with an ability to control, focus and concentrate on what is important. Failure to do this would result in the mind being overwhelmed by these stimuli and potentially leading to disorganisation.

There is another dimension to those who are physician-scientists and that relates to their roles as physicians who have confronted pain, suffering, death caused by various diseases and who see these as enemies. To fight these enemies, some would either do basic science research or disease-oriented research which is focused on understanding the pathogenesis or treatment of a disease, but does not require direct contact with the patient; others would choose

to do patient-oriented research where there is direct contact with patients.²⁴ It is this latter role as a “double agent” that gives that additional leverage in bridging research and clinical care but this blurring of boundary can also cause some blurring in thinking which can result in confusion or conflicts.²⁵ For a physician who provides only medical care, there is a convergence of the interests of the patient and of the physician which is to regain or maintain health, but in research these interests may diverge.²⁶ Physician-scientists are predominantly scientists and are therefore primarily interested in answering scientific questions about groups of patients. Because they conduct their research on patients, they are working at the knife-edge with potential ethical and moral problems. Just as patients participating in research may have “therapeutic misconception”, that is, the false belief that the intention of a research study is to directly benefit them,²⁷ physician-scientists may in their minds also think that the research is in the best interest of the patients, and may find it easy to tolerate or rationalise research activities that may compromise the well-being of the subjects.

In a moving and at times harrowing essay in the *New Yorker*,² Atul Gawande described the life and work of Dr Francis Moore, the youngest Chairman of Surgery in the history of Harvard Medical School. Among his many accomplishments, Moore also pioneered heart valve replacement surgery and organ transplantation surgery. Starting in 1951, he assembled a team and began transplanting kidneys into humans and by 1953, had transplanted kidneys in 10 patients. Every patient died within weeks, with the longest surviving 5 months. Despite widespread criticisms, he and his team went on to transplant kidneys in 15 more patients. All died. The tide changed only when it was done on a pair of identical twins where the donated kidney came from the healthy twin. The patient survived, recovered and married the nurse who looked after him. This spectacular success provided the impetus for Moore and others to continue, and their persistence resulted in tremendous strides in the science and techniques of organ transplantation and has made kidney transplantation into what it is today – an almost routine medical and life-saving procedure.

Gawande asked what kind of person could persist in inflicting “suffering and death because of an unproved idea, a mere scientific hope and repeated failure”. He cited the work by Renee Fox, a sociologist, and Judith Swazey, a historian, who have published many studies of the pioneers of surgical innovation. While they were generally “ruthless, bombastic, and unbending... self-absorbed and brutally competitive” and scornful of critics; they were also inspiring leaders. They took the “simple moral stance” that when people were going to die, not doing anything is not an option.

However, that was not easy – these pioneering surgeons have various ways of coping with the often appalling results of their experimentation: from a detached intellectualisation of the whole process, to the use of black humour of making self-deprecatory jokes, to spending anguished hours by the bedside of their patients. Gawande suggests that it was “their closeness to their patients that drove such surgeons to proceed as they felt that they were the only ones willing to do something for their patients who were dying and desperate.”

Francis Moore, himself, changed with time and in a latter article, took a decidedly cautionary position and articulated that there is no justification in taking whatever measures regardless of its degree of hopelessness in dying patients as it not only gave false hopes for them and their families, it also discredits biomedical science, and made physicians and surgeons as “adventurers rather than the circumspect persons seeking to help the suffering and dying by the use of hopeful measures”. However as Gawande commented, such caution carries a price particularly in a desperate situation where something or anything would have been tried and perhaps something new would have been discovered.

Mary-Claire-King, who discovered the genes for inherited breast cancer and inherited deafness, had said that people do science for 3 reasons—curiosity, altruism and ambition.²⁹ Ambition can, however, be treacherous. A seething and unrestrained ambition can have a self-delusory effect and subversively distorts judgment such that success is overestimated, risk is underestimated, and failures are explained away as exceptions. However, it may be more difficult – than most would think – to know or realise when this happens – when the pursuit of knowledge is about personal ambition and ego rather than doing what is right by the patients, and by science.

The path that a clinician-scientist takes is difficult and fraught with dangers. Joseph Goldstein and Michael Brown – both Nobel prize winners and clinician-scientists themselves wrote that physician-scientists have 4 things in common: a passionate curiosity, a deep involvement in the care of their patients, infinite patience, and being able to withstand poverty in terms of funding.²⁴ To which I would add what Henry Beecher wrote in his influential 1966 paper, “Ethics and Clinical Research” as a more reliable safeguard against unethical research, and that is the “presence of an intelligent, informed, conscientious, compassionate, responsible investigator”.³⁰

REFERENCES

1. Monmaney T. Marshall's Hunch. *New Yorker* 1993;64-72.
2. Kuhn TS. *The Structure of Scientific Revolutions*. 2nd ed. Chicago: University of Chicago Press, 1970.
3. Guilford JP. *The Nature of Human Intelligence*. New York: McGraw-Hill, 1967.
4. Simonton DK. Scientific creativity as constrained stochastic behaviour: the integration of product, person, and process perspectives. *Psychol Bull* 2003;129:475-94.
5. Andreasen NC. *The Creating Brain. The Neuroscience of Genius*. Washington DC: Dana Press, 2005.
6. Feist GJ. A metaanalysis of personality in scientific and artistic creativity. *Pers Soc Psychol Rev* 1998;2:290-309.
7. Amabile TM. *The Social Psychology of Creativity*. New York: Springer-Verlag, 1983.
8. Austin JH. *Chase, Chance, and Creativity: The Lucky Art of Novelty*. New York: Columbia University Press, 1978.
9. Roberts RM. *Serendipity: Accidental Discoveries in Science*. New York: Wiley, 1989.
10. Chang L, editor. *The New York Times. Scientists at Work*. New York: McGraw-Hill, 2000.
11. Swain JL, Stewart T, Leder P. Parental legacy determines expression and methylation of an autosomal fusion gene carried by a transgenic mouse. *Cell* 1987;50:719-27.
12. Allport G. *Personality: A Psychological Interpretation*. New York: Holt, Rinehart & Winton, 1937.
13. Nuland SB. *Doctors*. New York: Alfred A Knopf, 1988.
14. Juda A. The relationship between highest mental capacity and psychic abnormalities. *Am J Psychiatry* 1949;106:296-307.
15. Ludwig AM. *The Price of Greatness: Resolving the Creativity and Madness Controversy*. New York: Guilford Press, 1995.
16. Post F. Creativity and psychopathology; A study of 291 world-famous men. *Br J Psychiatry* 1994;165:22-34.
17. Barron FX. *Creative Person and Creative Process*. New York: Holt, Rinehart & Winston, 1969.
18. Rushton JP. Creativity, intelligence, and psychoticism. *Pers Individ Dif* 1990;11:1291-8.
19. Bachtold LM. Personality characteristics of women of distinction. *Psychol Women Q* 1976;1:70-8.
20. Barton K, Cattell H. Personality characteristics of female psychology, science and art majors. *Psychol Rep* 1972;31:807-13.
21. Getzels JW, Csikszentmihalyi M. *The Creative Vision*. New York: Wiley, 1976.
22. Rushton JP, Murray HG, Paunonen SV. Personality, research creativity, and teaching effectiveness in university professors. *Scientometrics* 1983; 5:93-116.
23. Wilson GD, Jackson C. The personality of physicists. *Pers Individ Dif* 1994;16:187-9.
24. Goldstein JL, Brown MS. The clinical investigator: bewitched, bothered, and bewildered – but still beloved. *J Clin Invest* 1997;99:2803-12.
25. Yanos PT, Ziedonis DM. The patient-orientated clinician-researcher: advantages and challenges of being a double agent. *Psychiatr Ser* 2006;57:249-53.
26. Miller FG, Rosenstein DL. The therapeutic orientation to clinical trials. *N Engl J Med* 2003;348:1383-6.
27. Appelbaum PS, Roth LH, Lidz CW, Benson P, Winslade W. False hopes and best data: consent to research and the therapeutic misconception. *Hastings Cent Rep* 1987;17:20-4.
28. Gawande A. *Desperate Measures*. New Yorker 2003;71-81.
29. Bass TA. *Reinventing the Future. Conversations With the World's Leading Scientists*. USA: Addison-Wesley Publishing Co, 1994.
30. Beecher HK. Ethics and clinical research. *N Engl J Med* 1966;274: 1354-60.