Sea-Change, Paradigm-shift and *Angst*

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Thomas Kuhn (1922 - 1996) considered the development of ideas in science, asserting that they took place not so much by steady research as by catastrophic changes in an underlying world-view. He gave currency to the phrase *paradigm-shift*.

He contended that members of a scientific community cannot communicate effectively unless they possess a shared set of received beliefs. A core belief-system is learned during the educational process, and adherence to it qualifies the student and equips him for a life's work within that community. The core system is not seen for what it is (a belief-system) but, rather, as an axiomatic framework; that is, an inter-connected group of self-evident truths. The ultimate aim is to use this axiomatic lens to gain an insight into nature itself.

Most research is actually not novel, but is centred on the augmentation (or even embellishment) of the prevailing paradigm: to sharpen, if you like, the focus of that axiomatic lens. It is an art which, by choice of subject, produces results generally favourable to the prevailing paradigm; these results are neatened to be archived within allowed formats. Research studies which produce anomalous results tend to be demoted, and, uncollated, are allowed to grow dusty on the shelves of stack-rooms.

With time, however, the number of anomalous results begins to rise. Workers distant from the establishment begin to link anomalies in unexpected ways. Establishment figures are reluctant to see this, and, indeed, are prepared to use increasingly arcane and elaborate systems of argumentation to support a cherished system: however, the time will come when the axiomatic framework will fail; it will no longer have credibility. This new thinking may be reinforced by the retirement of a generation of establishment thinkers. A paradigm-shift is about to take place. The new world-view is formulated and is put in place. Kuhn allows that the pain inherent in change is ultimately enriching to the body of knowledge.

But Kuhn's ideas are paradoxically vulnerable to their own style of argument. It is no accident that the idea of scientific progression by discontinuous paradigm-shifts has itself become an axiomatic framework; if this argument is correct, the integrity of that framework can only be temporary. What will replace it? Only the sharp-minded outsider can predict the next paradigm. Here Kuhn extended his hypothesis, and this extension is much weaker than his primary conclusions. His extension hypothesizes that 'axioms' are always illusory and can be no more than points of view and are only ever supporters of the collective psyche. This, in turn, implies that no scientific paradigms are truths, but are *always* akin to religious or political bodies of opinion. This doesn't fit facts. Consider, within evolutionary theory, the case of endogenous retroviruses in mammalian genomes: if you don't think that their arrangement posits solid evidence for an evolutionary divergence of species then you have not understood the case. Consider also, against this, the scientific dictum that solid evidence can never do more than approach an asymptote: it is never proof.

Multiple Sclerosis: cause and treatment.

There is abundant evidence that, at its root, MS springs from a genetically-determined reaction to a common chronic infection under certain environmental conditions. The manner in which the neurological establishment (which holds the view that MS is an autoimmune process) has dealt with this evidence fits in remarkably well with Kuhn's ideas on how establishments seek to down-grade and demote strong information inimical to the prevailing axiomatic framework, while simultaneously promoting even weak information which is supportive of it.

There is no doubt that MS is a mysterious and complex illness: in the history of its scientific investigation there has already been one large paradigm-shift. In the nineteenth and early twentieth an infection model prevailed. Epidemiological observations tallied with this. This infection model continued with Dr Paul Le Gac, a Belgian physician who found evidence of antibodies to intracellular organisms in the CSF of persons with MS in the 1950s and 60s; many of these patients did well when treated with broad-spectrum tetracyclines. His work seems to have been the last in that epoch: the paradigm-shift to autoimmunity had already begun with the acceptance of experimental allergic encephalopathy (a disease induced in animals) as an inexact autoimmune model. Now another major paradigm shift is about to take place. It is a return to the infective model. A dozen or more potential pathogens have been mooted. It is possible that the infection is polymicrobial, as is becoming apparent in chronic infective arteriopathy. These ideas had been in the air for some time. Tumour Necrosis Factor α, for instance, was found in the CSF of people with active but not inactive MS in 1991; TNFα is a cytokine fairly specifically induced by bacterial endotoxin; indeed, in the 1890s the physician William Coley was able to successfully treat metastatic malignancy (in a proportion of cases) by

inducing TNFα using a bacterial vaccine. A very specific breakthrough in the understanding of chronic infection in MS was gained with the culture of *Chlamydia pneumoniae* from the CSF in 64% of persons with MS, and demonstration of chlamydia-specific gene-sequences in 97% of these persons by Dr Charles Stratton and colleagues at Vanderbilt University, Nashville. This key paper was published in 1999. Further studies (using sensitive methodologies) have confirmed these findings.

Kuhn posits angst at a personal level as group paradigms are challenged. This appears to happen in the example of MS causation and treatment. Many neurologists become angry when an ongoing infectious cause for MS is mooted, even when a patient is recovering on an antimicrobial regimen and has been saved from a situation of complete dependence. One neurologist refused to look at the improved follow-up MRI of a recovering patient when the radiologist was about to place a film on the light-box. He apparently held up his hand and exclaimed 'I can't see it!' Another neurologist told a patient with primary progressive MS not to darken the door of his office again after she had commenced antimicrobial treatment. Her EDSS had improved from 6.7 to 2 on his own assessment (an improvement almost unknown in the natural history of untreated disease) but he had no wish to examine the cause of that improvement. Kuhn seems to be right in this as well: truly we are wedded to our paradigms even at the expense of our humanity.

What will happen in the future? It is hard to see any further paradigm-shift of equally monumental proportions in the causation of MS. There will be changes of thought within the infective thesis. Certainly, the disease will be diagnosed earlier, will become less problematic; antimicrobial schedules will be hotly debated. Cofactors will be discovered. Immunomodulation will be explored in those subsets where chronic infection has given rise to real autoimmunity. Molecular mimicry will be explored. Immunization possibilities will be explored also. But the motor of infectious causation seems to have been broadly settled.

And so Kuhn is partly correct; he is right in that paradigm-shifts can occur successively. But I think that he is not *au fait* with the nature of science. Paradigm-shifts occur, certainly, but only until one reaches a core which is demonstrably realistic, as is shown when concordant evidence has been gathered in the various languages of different disciplines.

As a scientific path develops, its 'axioms' have many political or religious qualities in that they resist as best they can any perturbing examination, but, when the quiddity of the underlying mechanism is grasped, that path at last enunciates knowledge.

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