Coda

Medical reductionism: lessons from the great philosophers

Recent years have seen significant improvements in the treatment of disease, many of which are the result of a better understanding of the intricate components and processes involved in cell biology. For example, our knowledge of cell proliferation pathways is becoming ever more detailed leading to the development of an increasing number of novel targeted therapies. Medicine is following a philosophy of ‘reductionism’: deconstructing a complex process into its component parts to enable better comprehension. Although this approach has obvious advantages in that identifying specific component malfunctions might lead to more effective and less toxic treatments, there are potential dangers in becoming too reductionist in our philosophy. The advantages and disadvantages of reductionism have long been debated by philosophers and thinkers and there is much to learn by revisiting some of their arguments with reference to the field of medicine.

The history of reductionism

The earliest reductionist philosopher was Thales, born around 636 BC at Miletus in Asia Minor. He hypothesized that the universe was made out of water—water being the fundamental substance of which all others were composed. Reductionism was later re-introduced by Descartes in Part V of his Discourses.\(^1\) He suggested that the world was like a clockwork machine, which could be understood by taking it to pieces and studying the individual components. Reductionism has since developed to encompass at least three related but distinguishable themes: ontological, methodological and epistemic. In biological science, ontological reductionism is the idea that each system is constituted by nothing but molecules and their interactions and also establishes a hierarchy of chemical, biological and physical properties. Methodological reductionism is the idea that biological systems are most fruitfully investigated at the lowest possible level and epistemic reductionism suggests that knowledge of a higher domain can be always reduced down to a lower more fundamental level. In modern cancer research, it is often methodological reductionism that predominates.

There are, however, potential problems with a reductionist approach:

(i) Reductionism often arouses distrust: although reductionism aims to make things more intelligible, in reality the common understanding of the many tends to be replaced by the better understanding of the few. When a disease is explained in molecular and submolecular levels, it becomes difficult for the layperson to conceptualize. We see this in medical science, where even dedicated researchers are unable to have a full understanding of the cellular pathways outside of their immediate field of interest.

(ii) Reductionism risks oversimplification of a process: in reducing something down do we merely eliminate certain aspects from our description of it? There becomes a point where the reduction becomes disassociated from the phenomenon it is trying to explain and exclusively reductionist research strategies can be systematically biased and overlook salient biological features. Again this is evident in medicine—although many ‘targeted’ agents are now used in the clinic, it is fair to say that in most cases the benefits to patients have been relatively modest, despite sound theoretical principles and laboratory data.

(iii) Reductionist explanations can sometimes lead to confusion over cause and effect: this is the classic ‘chicken and egg’ problem. For example, is a disordered proliferation pathway the cause or result of a malignancy—which came first? We may not be targeting the root cause of the problem.

Holism and emergence

The opposite of reductionism is ‘holism’. This approach is traced back to a statement made by Aristotle in his ‘Metaphysics’:\(^2\) ‘The whole is more than the sum of its parts.’ For our purposes, we could interpret this as ‘disease is more than the sum of disordered enzymatic and cellular interactions’.

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Unfortunately, the term ‘holistic medicine’ has been somewhat hijacked by alternative therapists and is often thought mistakenly to be at odds with conventional medicine. What it really means, of course, is looking at the patient and disease as a whole rather than focussing on interactions at cellular levels.

A key assumption of the holistic approach is that there are ‘emergent properties’ on the progression from a lower to a higher hierarchical level—things that cannot be explained by examining the component parts themselves. Stuart Kauffman describes three examples of emergence—life, agency (or decision-making ability) and consciousness— all of these are transitions that cannot be explained simply by linear interactions. A classic example of emergence in science comes from the study of atoms and the higher hierarchical level of molecules. The chemical bond is a major part of molecular science but does not exist in the world of atoms and, no matter how hard an individual atom was studied, these bonds would not be discovered. In the field of genetics, Hull argues that it is impossible to reduce population genetics to Mendelian genetics because the higher level is a result of many entities interacting at the lower level that could not be predicted by studying the lower level alone. Similarly there may be emergent properties that are being overlooked in the increasingly sophisticated and reductionist study of cell biology. Disease in humans can never be fully understood in the laboratory. This highlights the importance of communication between basic science researchers and physicians through appropriate translational research projects.

Evidence-based reductionism

It is not only in the laboratory where reductionism pervades. The evidence-based medicine (EBM) movement has effectively taken over as the dominant force in medical research, from the design and reporting of trials, through the development of treatment guidelines to the funding and commissioning of new drugs. However, the generally accepted universality and objectivity of EBM comes at a cost—clinical problems must be defined in heavily simplified terms to enable randomized controlled trials and meta-analyses. This reductionism requires complex entities to be simplified as quantitative units to which statistical methods can be applied. Clinical researchers constantly strive to subdivide patients into defined groups in order to test which will benefit most from a particular treatment option. The uniformity of practice that ensues might be too crude to apply to an individual patient’s experience. This is not to detract from the admirable moral standpoint of EBM which, when universally implemented, should maximize health gain across a population. Jeremy Bentham, the 19th century philosopher and father of utilitarianism, would be proud of this enterprise to provide ‘the greatest good for the greatest number’ but inevitably, as with any utilitarian approach, there will be some patients who are not best served.

There is an interesting asymmetry developing whereby meta analyses are entrusted to special centres far removed from the majority of practicing doctors. The results of these systematic reviews are propagated as objective unbiased findings upon which guidelines and commissioning decisions are based. It may not be good practice, or even ethical, to manage individual patients according to these reductionist protocols without regard to their individual circumstances. The reliance of commissioning on EBM and the associated economic parameters (such as quality-adjusted life years) is particularly worrying. It is impossible to accurately reduce the benefit of a treatment into a simple equation of cost and survival, particularly in the case of chronic or terminal diseases. There are so many more factors to take into account, such as the availability or lack of alternative treatments, psychological issues, family and dependents, timing of diagnosis and disease progression, pre-existing quality of life and so forth. Inevitably commissioners, governments and insurers are obliged to assess specific outcome measures to judge the utility of a therapy, but the current tools are reductionist and do not adequately represent the overall benefit to patients.

Reductionism in the clinic

The Chaos Theory has been popular in the physical sciences for some time, but has only really been applied to the social sciences since the mid-1990s, initially by Barton in the field of psychology. It highlights the interdependency among variables and the overall holistic patterns that emerge from these dependencies. In basic medical science, these interdependencies are becoming better recognized—cell proliferation is dependent on multiple growth factor receptor pathways, angiogenesis, apoptosis and cell migration. In cancer medicine, it is not sufficient to block just one of these pathways if malignant cell growth is to be halted completely. In a similar way, the choice of treatment is not only
dependent on tumour factors such as size, grade, receptor status and stage, but also on patient-related factors such as age, performance status, co-morbidities, prejudices, social situation, mobility and many others which are not all accounted for in protocols and guidelines. This is of course where the art of medicine comes in. Although protocols can be helpful in directing therapy, it is easy to over-interpret their value in decision making for individual patients.

The media tends to propagate reductionist views in medicine with over-simplistic headlines such as ‘New cure for Alzheimer’s’ or ‘Cancer gene identified’. These articles give patients the idea that a simple one-step process can be targeted in the treatment of disease, when clearly there are multiple factors involved. Allied disciplines in medicine such as nursing, which have traditionally taken a more holistic approach to the patient, are also in danger of becoming reductionist. There are tendencies towards more specialized roles, which might detract from caring for the patient as a whole. There have, however, been some encouraging moves away from reductionism. Survivorship programmes intend to address lifestyle changes following diagnosis of disease, bringing in aspects of diet, exercise, financial planning, psychological support and so forth. Again, a cautionary note must be flagged. There is a danger that aspects of this approach may become reductionist in themselves, such as relating the disease to specific dietary components, and this in turn may have a negative influence on the patient’s future quality of life.

**Statistical reductionism**

Many renowned scientists argue that science in general must be better at studying larger scale organizations and how they influence the lower levels of organization. This ‘network’ approach is most extensively studied in information theory which utilizes applied mathematics and electrical engineering to measure interaction and levels of uncertainty, specifically applied to the internet and other interconnected communication systems. There is some interest in applying similar techniques to medical science. Rather than inputting specific closed questions as we do with conventional statistical analysis, the network approach looks for patterns and trends. It could be described as a holistic version of conventional reductionist statistics and might bring to light emergent associations that are currently being missed.

The philosopher Karl Popper developed the ‘propensity theory’ which states that the outcome of an experiment or action is reliant on a set of ‘generating conditions’. The relative frequency of achieving the outcome $E$ for this set of conditions is defined by the propensity $p$. It is easy to see how this principle could be applied to medicine, where for each set of conditions (disease factors, performance status, co-morbidities, etc.) any given treatment schedule would have a propensity $p$ of resulting in a cure $E$. Although this is essentially what we as physicians do each time we see a patient, it is difficult if not impossible to quantify these values. Attempts have been made across various medical specialities to provide computerized prognostic or ‘relative frequency’ tools, but these result in a necessarily reductionist approach due to the restrictive nature of data input. A very limited number of disease and patient-related parameters are entered into an algorithm, yet the figures generated by these tools, often to within tenths of a per cent, are misleading in their precision and can be confusing to patients, particularly those unfamiliar with probability.

**Greedy reductionism**

Daniel Dennett introduced the idea of ‘greedy reductionism’ in his book entitled ‘Darwin’s Dangerous Idea’ published in the mid-1990s. There is a tendency to feel that every explanation in every field of science should be reduced all the way down to cellular biology and particle physics. Dennett points out that the lowest level explanation of a phenomenon, even if it exists, is not always the best way to understand it. John Maynard Smith, a famous evolutionary biologist, summed up the reductionism/holism debate with the following statement: ‘...Holists are, I think, in a weaker position, if only because progress has been so much faster from the bottom up than from the top down. Yet I do share their conviction that there are laws that can only be discovered by research on whole organisms and populations of organisms.’

**Conclusion**

Although it would be naïve to ignore the strengths of a reductionist approach to the study of the disease process, it seems that something is being lost in the translation from theory and laboratory to the clinic. In medicine, we are in danger of becoming greedy reductionists and it would pay for us to step back...
occasionally and take a more holistic view of our field.

Mark J. Beresford

References


