PERSONAL VIEW

The limits of medical science

Bernard Brom

If there are limits to what can be known then it seems we need to be very cautious in believing that what is known is the whole truth. If it is not the whole truth, then it may even be untrue and just a good story, which may seem to be true only under specific circumstances.

The rapidity with which science has advanced has created the idea that there is clockwork-like certainty around the way the universe goes about its business and that this can and will be measured with a great degree of accuracy. Although this idea is held by many scientists, there is an increasing understanding that within nature there is also a great deal of uncertainty and unpredictability. Bruce West, a physicist at the University of California, and Ary Goldberger, a Professor at Harvard Medical School, in an article in the *American Scientist* state: 'The variable, complicated structure and behaviour of living systems seem as likely to be verging on chaos as converging on some regular pattern.'[1]

The fact is that turbulence, irregularity and unpredictability are now recognised to be everywhere and will constantly confound all our efforts to make absolute sense of the world. Chaos theory as formulated by physicists does not suggest that the world is chaotic, but only that so much is happening in every moment of time that any attempt to predict the future is fraught with problems and 'unpredictability'. Our attempt to predict the weather is a perfect example of this fact. Some scientists have even abandoned the idea that a 'universal field theory' will eventually be found incorporating all the known laws of science into one universal theory in which 'the mind of God' will become a formula on a piece of paper.

All this has important relevance to the science of medicine and may explain the variability encountered in medical trials and why one may never find absolute answers. In the meantime, the call is for 'evidence-based medicine'. This article questions whether the latter is truly possible or whether it is just another scientific dream.

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Order and disorder

Order suggests that everything is in its right place and functioning well (Collins English Dictionary). What is the secret of that order, where are the controls and how does disorder arise within that system? The underlying idea behind the concept of a universal field theory, which would explain everything, is that there is order in the universe. Chaos theory does not suggest that chaos exists but only that there are so many things happening in every moment of time that it becomes impossible to measure them all. So, despite apparent randomness and chaos there appears to be an underlying order. It was to this order that Einstein referred when he commented that God does not play dice with the universe.

It was Edward Lorenz, a meteorologist, who introduced the concept of 'chaos theory' and the 'butterfly effect'. One evening after doing research into weather prediction using theoretical numbers to the sixth decimal place, he decided to check these figures and run the numbers through again. Because he was in a hurry, he shortened the numbers from six decimal places to three decimal places. To his astonishment, the computer came up with a completely different weather prediction. At this point he made a statement epitomising the new science: 'I knew right then that if the real atmosphere behaved like this [mathematical model], long-range weather forecasting was impossible.' He realised that if the results were so far apart (when comparing figures to the third or sixth decimal place), then 'complex non linear dynamic systems such as the weather and man must be so incredibly sensitive that the smallest details can affect them'. Small changes have massive effects. A butterfly flapping its wings in New York may cause a storm in San Francisco. On a weather map, a meteorologist is unable to predict which irregularity will explode into a storm. So, while there appears to be an underlying order there are so many factors involved and such sensitivity that prediction is impossible.

Cause and effect

The conventional viewpoint is that for every effect there is a

preceding cause. This linear way of observation and scientific investigation is often referred to as the Newtonian approach. Linear physics suggests a universe run by underlying laws, which govern the way everything functions. According to this approach, a study of these laws would eventually define the workings of the universe. 'Nature and Natures laws lay hid in night. God said, "Let Newton in!" And all was light.' (Alexander Pope, 18th century English poet.)

Quantum mechanics, however, introduced scientists to the fact that non-linear dynamics is a fact of life and that cause and effect are not so clearly related. 'In the nonlinear world — which includes most of our real world — exact prediction is both practically and theoretically impossible. Nonlinearity has dashed the reductionistic dream.'[2] '. . . May God us keep from single Vision and Newton's sleep'. (William Blake.)

Most practitioners today recognise that there is in fact no single cause of ill health. Bacteria do not cause tonsillitis without there being a susceptibility. The susceptibility is dependent on numerous factors including genetic, environmental and emotional/mental factors. The ability of the body to respond and the way it responds is also dependent on a whole range of factors. An attack of tonsillitis is a highly complex interaction between the individual system and all that keeps it healthy, and the invading bacteria.

There are in fact so many factors involved that one cannot strictly speaking talk of a cause, but rather of multiple factors in a highly complex system. Biological systems are in addition open systems, which means that they are not separate from the environment but are open to environmental factors. The latter includes not only a host of toxins in the environment, but also many other factors such as noise level, electromagnetic pollution, weather conditions, building syndrome conditions, underground water, cosmic conditions and many other unknown factors. These unknown factors themselves may be vitally important and condition the way the living system responds.

The fact that biological systems are open systems also means that in some known and unknown ways each system is connected to the world and even to the universe around it. This connection is essential to its survival.

What we see is what we look for

In the quantum world, the observer plays a crucial role and cannot be left out of the experiment. The very act of taking part in the experiment seems to change the course of the experiment. This was clearly shown in the two-slit experiment. Suffice to say that the way the experiment is set up creates the endpoints. A sausage machine makes sausages out of meat. The size and shape of the sausages depends on the machine. Light is regarded as having particle or wave properties. What makes the difference is the observer who sets up the experiment and the instruments used. Can light really be measured or do we merely extract from light (or create) a wave or particle effect? The way we set up the experiment defines the endpoints.

Statistics

Statistics developed to try to make sense of chaos, of a universe that seemed unpredictable and in which there appeared to be an enormous number of facts to deal with. Good weather forecasting is both a science and an art. However, there are rapidly diminishing returns as one looks into the future. The world is exceedingly complex and statistics at its best is a good guess, but again with rapidly diminishing returns.

This often seems to be borne out in the real world of medicine as well. Wonder drugs are routinely disappointing, 'clinically proven' therapies continue to fail over time, and major breakthroughs seem to lose their lustre. Is this a major problem of the statistical method, or the result of the underlying chaos in which prediction is in fact impossible? The statistical method does have major problems. Firstly it is dependent on the material gathered, which may be inappropriate; secondly unusual results are often left out because they seem to disturb the smooth curve of the graph; and thirdly the very method itself may be fundamentally flawed.

'. . . some of the world's most distinguished statisticians have been warning for years that these techniques routinely exaggerate the size and significance of implausible findings . . . these techniques will see "significance" in results which are in fact the product of chance.' Further on the author states that the results can easily double the real efficacy of a useless drug.[3]

Double blinds and evidence-based medicine

It has become increasingly obvious that biological systems and the world itself do not function like clockwork, with every effect preceded by a simple cause. Nature is 'relentlessly non-linear' and non-local and this appears to be a property of the entire universe.[4] One of the properties of non-linearity is that it goes in all directions and all its relationships are also non-linear. In order to understand this clearly we can no longer think in terms of parts but rather in terms of systems, and open systems at that. Human beings are not made up of parts but each human being is an open system — complex and dynamic. Systems flow and self-regulate. No two systems function in exactly the same way. No two human beings will feel well eating exactly the same food, drinking the same water, doing the same exercise, and subject to the same emotional and mental pressure. Nor will they have exactly the same levels of sodium, potassium, cholesterol, etc. — they will be

approximately similar with regard to some levels and widely different in others, even when healthy.

Chaos theory has also indicated that these self-regulating systems have a deeper level of order and that there is a clear relationship between order and what appears to be disorder or turbulence. Turbulence may in fact turn out to be the very way that leads to the sudden emergence of new forms of order in nature.

Acute disease may turn out to be the form in which turbulence expresses itself in the system, an attempt to move the biological system to a higher level of functioning. Attempts to control this process may be counterproductive and it may be much more useful biologically speaking to let the system continue its processing and only intervene if there is a danger of the system self-destructing.

'Another important property of nonlinear equations that has been very disturbing to scientists is that exact prediction is often impossible.'[5] This has already been mentioned in the discussion on weather prediction. In medical research and evidence-based medicine statistics are being used to try and find patterns that may give some predictive value. Because every researcher and investigator has his or her own bias, the tendency is of course to find what one is looking for.

A number of assumptions can perhaps be made from the above discussion.

1. Human beings are complex open systems.

2. What appear as symptoms and signs are the result of multiple underlying influences on the complex system.

3. The symptoms and signs are also the result of the way the system responds to these multiple influences.

4. There are no parts in the system. The whole system is always responding in order to maintain harmony.

5. Acute disharmony or distress in the system may be similar to turbulence or a period of chaos in which the system attempts a re-adjustment. This may have evolutionary consequences.

6. There appears to be a whole range of unknown factors, which cannot be measured. These may not be measurable because they lie buried within the complexity of the system. Any attempt to identify what these factors are disturbs the system. Or these factors may not follow linear processes and therefore are impossible to identify.

Any attempt to understand what is going on and why medical research is so full of contradictions and anomalies may depend on our ability to live with the unknown. By the end of the nineteenth century, it was quite common for scientists to believe that all the major questions of physics were close to resolution. 'It only remained to carry measurements to the higher degree of accuracy represented by another decimal place, and to frame some reasonable credible theory of the structure of the aluminiferous ether.'[6]

There is a tendency among many scientists to believe that we are now at a point where science is almost able to combine all the laws of science into a single formula.

Perhaps we need to ask whether this is in fact true, or whether what we know is only a small part of what can be known. For while we have created stronger and even better drugs and better surgical techniques, the underlying causes of most illness remain unknown. Even Niels Bohr, a Nobel Prize winner and one of the greatest physicists of our time, felt very humbled by some of the truths emerging from quantum mechanics. He described reality as being 'far more complex than we had anticipated', and said that beneath all appearances of solidity there was only the 'seething, unimaginable quantum flux and this could not meaningfully be said to look like anything'.[7]

What is this unknown and how does it influence what we know? If what we know is 'almost' all that can be known, then one would expect that what we know is good enough, but in fact this does not seem to be the case. Uncertainty, turbulence, and chaos are a fact of nature and therefore all systems are potentially unknowable. It could also be said that what we know is a very small part of what there is to know, in which case the information we have is very unreliable. We like to think of course that we know a reasonable amount of what there is to know so that our deductions, conclusions, concepts and approaches to treatment are reasonable. This may, however, be extreme arrogance because without knowing all there is to know there is no way of knowing whether what we know is true. With treatment generally being symptomatic, causes of ill health remaining elusive, and iatrogenic disease on the increase we may conclude that our conventional story around health and disease is probably far from the truth and may therefore be untrue.

With so much unknown and unpredictable, it would be a grave error to believe that we have or even can have a real handle on disease and even health. In their article on evidence-based medicine and the treatment of sore throats with antibiotics Dr Kali and Professor Swingler conclude that 'An evidence-based approach does not replace clinical judgment. It is merely a tool to improve that judgment and the well-being of the patient.'[8]

It is not surprising that evidence-based medicine is not enough. The most characteristic feature of people taking part in a trial is not what they have in common but their absolute individuality. We do not have a group of normal individuals versus a group of sick individuals. We have 100 or 1 000 or even 10 000 individuals regarded as normal who have very little in common with each other unless one creates artificial categories with criteria broad enough to fit them into. Each so-called normal individual has his or her own levels of sodium, potassium and cholesterol, as well as different liver function,

immune system criteria, sedimentation rate, white blood cell count, length of nose, shape of stomach, skin and hair colour, etc., all of which characterise that individual, making him or her unique. Choose another 100 or 1 000 or 10 000 subjects and one has another group that may be called normal but that consists again of a group of individuals totally different from any other group. No wonder researchers have to keep repeating one drug trial after the other to try and come up with meaningful results.

Conclusion

The real world of biological systems is cut through and through with chaos, unpredictability and turbulence, making absolute prediction impossible. The limitation of science is the recognition that the unknown will remain the unknown and will continue to confound us, and any effort we make to be in control.

It is not that evidence-based medicine has no value or that experience is more appropriate. It is just that the humility to recognise how little we really know is a good approach at this time if everyone is to work together for the greater good of the sick person.

'Our knowledge about the universe has an edge. Ultimately, we may even find that the fractal edge of our knowledge of the Universe defines its character more precisely than its contents; that what cannot be known is more revealing than what can.'[9]

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IN BRIEF

Use of sildenafil for ED classes II and III

Erectile dysfunction (ED) is common in patients with congestive heart failure (CHF), and is often associated with depression. Using sildenafil (Viagra; Pfizer) for ED in men suffering from CHF has been contraindicated. But a recent prospective, placebo-controlled, double-blind cross-over trial has proved that it is a safe treatment. Thirty-five patients participated in a 12-week trial — inclusion required a history of ED and absence of ischaemia (negative results from exercise stress test or nuclear perfusion scan) or nitrate use. The participants received 50 mg sildenafil and its tolerability was determined by measuring the ambulatory blood pressure for 4 hours after a single dose. Improvement in ED was assessed by the International Index of Erectile Function survey. Improvement in depression, mood and quality of life was also assessed. It was found that sildenafil caused a mean decrease in blood pressure (± SEM) of 6 ± 3 mmHg, and that ED scores were improved. The investigators concluded that sildenafil was a safe and effective treatment for ED in men with class I or II CHF, and provides relief of depressive symptoms.

(Webster LJ *et al.*, *Arch Intern Med* 2004; **164:** 514-520)