THE INTERPRETATION OF ILLNESS: ORCHESTRATING DISEASE

JOHANNES BORGSTEIN

> Since we can never know all the factors involved in an issue, we can never resolve it.
>
> Fernando Pessoa

> The reason why physics has ceased to look for causes is that, in fact, there are no such things. The law of causality, I believe, like much that passes muster among philosophers, is a relic of a bygone age, surviving, like the monarchy, only because it is erroneously supposed to do no harm.
>
> Bertrand Russell

IS ILLNESS CAUSED BY A MISINTERPRETATION OF ENVIRONMENTAL INFORMATION?

Cartesian tradition in medicine considers the body as a machine, and the physician as mechanic or at best an engineer, correcting the damaged sprockets, exchanging pieces and injecting a little oil or antibiotics here and there. This biomechanical model has served us well, but its limits are being felt, and just as Newtonian physics had to make way for newer theories, so will the venerable biomechanical model. The exceptions and failings are becoming impossible to ignore and we must explore alternatives. There is, however, a dilemma, for the alternatives hold not only serious consequences for medicine, but threaten to break down the very structure of scientific research in the biomedical fields.

Biomedical research has for the past centuries been based firmly on the principle of determinism; of absolute causality, in which we are convinced that if we search long enough we will find a single cause for any particular condition. Claude Bernard, who wrote probably the most complete and lucid analysis of the scientific process in his classic text “The introduction to experimental medicine,” reaffirmed repeatedly that the only thing holding together the concept of scientific medicine (against the vitalists and empiricists trends of his day) was his absolute confidence in (absolute) determinism. Everything else is open to doubt, should be open to doubt; frequently he would overturn an elegant hypothesis on the evidence of a single experimental fact.

Erasmus University Rotterdam, AZR-Sophia, Dr Molewaterplein 60, 3015 GJ Rotterdam, Netherlands / borgstein@knos.azr.nl jborgstein@yahoo.com

Ludus Vitalis, vol. IX, num. 15, 2001, pp. 229-235.

This is where the problem arises. For a long time we were able to persuade ourselves that incongruencies in the research results were due to the extreme complexity of the biological organisms, that perfecting our statistical methods would somehow give us the information we were looking for: the linear causality of the physical sciences, where every effect has a cause. In clinical medicine we were even able to convince ourselves that statistics were a suitable substitute for reality, though Bernard already warned against them, and realised that where the cause was clear the need for statistics never arises, that they need only be employed where no certainty exists. Mathematics assents that the "law of large numbers" is always valid in general and never in particular. No amount of statistical analysis will allow us to predict what number the next roll of the dice will turn up, or if the next patient will recover or die from his operation. Statistics is an elegant means for disguising our ignorance. Why then are even the most sophisticated molecular biology methods still faced with uncertainty? Why can we so rarely find a single cause for illness? Why does medicine so stubbornly refuse to become pristinely scientific?

We must then consider a number of possible alternatives:

1. Biological systems are so complex that we may not be able to encounter a single cause for every phenomenon (*complexity of cause*).
2. Fragmentation of a biological system during research, reaches a point where we can no longer extrapolate research results to the whole organism; results obtained for a fragmented or subdivided unit are not valid for and cannot be extrapolated to the whole organism (*fragmentation enigma)*.
3. Biological systems have a limited number of possible expressions of malfunction, so that different stimuli may produce the same effect, and cannot be distinguished on effect alone (*convergence of effect).*
4. The system may respond in various ways to a similar stimulus *(divergence of expression).*
5. There is no single clear causality for many biological phenomena; biological systems are not deterministic in many of their functions (*non-determinism).*

Let us analyse some of these points in more detail. Illness is often caused by a combination of factors, though their interactions may be so complicated that we will probably never be able to discover all of them.

As we ascend the biological complexity scale, it becomes progressively more difficult to unravel the systems, until we reach a point where the interactions are so delicate and intricate that their very unraveling alters such interactions and prevents their correct interpretation. The forms in which a malfunction or damage can express itself are from any particular level of perspective limited. Several different causes may produce similar symptoms, just as one stimulus may produce multiple responses. If we define a single cause for a phenomenon, or assume a constant response, we will be mistaken in part. We may however be correct in some other fraction, and statistics can then help to precise those proportions—for the whole group, never for the individual—and thus become a useful instrument of prediction.

Many of these objections are tackled by the current scientific methods, and it is argued that with refined techniques we will be able to perfect less invasive methods and detect ever more subtle physico-chemical changes in the metabolism. Both these contentions are partly correct, and are used to justify ever more complicated and expensive analytical methods, as has occurred in the physical sciences, which continue to advance with some success, though at a tremendous expense.

The last point mentioned above, non-determinism, takes us further out of the realm of traditional science entirely, and somehow threatens the very structure of scientific concepts and methods in the biological sciences. *There is no determinism in biological systems. Any biological structure, from the cell upwards, interprets rather than responds directly to a stimulus.*

If you kick a rock (to borrow Samuel Johnson's famous example) you will hurt your toe. The movement of the rock and the energy returned to your foot can be exactly calculated and will be constant under the same conditions (though the pain is entirely subjective). Step on a dog's tail*, and a whole range of possible responses may result. The dog is quite likely to bite you on the leg, or jump out of the way, causing you to overbalance and fall, or perhaps both. Your daughter will not speak to you for a week, and the neighbors may never speak to you again (if it was their dog), you may even receive a legal citation from the animal protection society. The effect does not depend directly on the stimulus, but on the interpretations of this stimulus. The more complex the organism, the less predictable and less constant the response; even single cells respond in varied ways. The only really predictable result is the loss of function of a dead cell, which reverts to chemical responses and reactions.

The difference lies in communication. Inorganic matter reacts to a stimulus in a constant way, entirely predictable within the physico-chemical model, if we unravel the situation sufficiently (until we reach atomic levels, where the uncertainty principle kicks in). The cell or organ or organism (this may even be extrapolated to social groups of organisms), receives information from the environment (interior or exterior), which it processes to produce a response. There is no direct deterministic response, but a series of possible responses which at cellular level the genetic material modulates, and which modulate the genetic material. There is

---

*As with Schrödinger's cat, this is exclusively a thought-experiment—do not try this at home!

information processing at different levels which is essentially different from the reactions produced among inorganic matter, so that we obtain the illusion of a direct deterministic response only because a similar stimulus is often processed in a similar way, but at times there may be a difference in the processing and the result is unexpected. The interaction of several biological entities obviously complicates the whole process still further, and will throw up unpredictable results with certain indeterminable incidence.

Cancer growth in this model is really the result of a communications breakdown. The normal cell differentiates and grows to a functional level, largely under 'environmental' influences, which determine its growth, differentiation and specialization. These influences may be chemical, hormonal, neural or even physical, and depend on the cells position and situation within the body. Neighboring cells will modulate their growth and differentiation to produce coherent organs that function together to form an organism, which must in turn function within the external environment. All these processes are based on the interpretation of the direct and indirect environmental factors. This interpretative process has more in common with linguistic mechanisms than the deterministic systems of the natural sciences, where there is no interpretation of a stimulus.

A cell may produce neoplastic growth if the information from its surroundings becomes confused, blocked, or misinterpreted. Environmental causes (such as a chronic irritation) may send chemical or physical information to the cell which interprets it as a growth or de-differentiation stimulus. The controlling stimuli from surrounding cells may be prevented from reaching the interpretative mechanisms so that the cell division is not halted in time, or alternatively, the genetic and cellular mechanisms may be damaged, so that part of the environmental factors are no longer taken into consideration. There is then no clear cause and effect, but a breakdown in the normal communication systems.

Similarly, the immune system responds to information it receives. If the interpretation is faulty, an innocuous chemical or pollen may induce an allergic reaction, whereas if it fails to interpret the information of a bacterial contamination, and responds below optimal levels, an invasion may result. A specific bacterium will not produce illness in all patients, or even in the same patient under different conditions. The way each patient responds in case of illness is also variable. There are always, no matter how virulent the bacterium, a proportion of patients who will interpret the aggressor correctly and respond adequately, just as a particular bacterium may find the conditions unsuitable for growth and division.

Just as no two persons will interpret a text in the same way, no two cells will interpret the environmental factors in exactly the same way, and thus no two cells will ever develop in exactly the same way. The interpretation is often similar or we would not be able to use language, and the majority of the cells will respond adequately to the stimulus or the organism would be unable to develop coherently. If the stimulus is of an unrecognised type (unknown language) the variety of interpretations are much wider, and if the interpretative mechanism is damaged (aphasia), the results are even less predictable. The cellular mechanisms then may vary in their response to a specific stimulus. No direct or predictable determinism exists. Only the interpretation can be analyzed (and statistically quantified). The responses are fairly constant, and variations are often not enough important to affect the conjoint functioning; nevertheless, ocasionally a communication error, a misinterpretation, may result in an important breakdown of function that leads to disease, as when a misunderstanding in a conversation leads to a quarrel. However, since absolute determinism is the basic precept of science, this puts in question much of biological scientific research.

To advance further, we may need to reinterpret biological function in terms of information and chaos theories.

Biological structures are made up of large numbers of different cells that somehow interpret the information offered to them by the environment in a functional way; in such fashion that allows the whole to continue functioning. Being so, their individual functioning must be similar, without ever being identical. No biological cell is ever identical to any other cell. Since such variety could not possibly be coded into the genome, it implies that cells develop according to an environmentally modulated genetic pattern. Similar cells interpret the various environmental influences and offer globally similar but slightly different responses. The whole is somehow coordinated, orchestrated perhaps, to provide a predictable result within fairly narrow margins.

The orchestra metaphor is useful to capture some of the interactions during illness. Everything sounds fine until perhaps a string breaks, and the orchestra must adapt its function rapidly, if it is not to degenerate into chaos or grind to a halt. Many factors are involved, and the result is not entirely predictable. To take the metaphor a little further, we cannot imagine the orchestra and everyone of its members always playing exactly the same piece in exactly the same manner; it is precisely the minor variations that give flavor (if I may be allowed that synergism) to the performance, which allow a varied response to unusual or uncommon stimuli.

While every cell participates in a harmonious way the body is in health, but if some cells, under whatever stimuli, suddenly play a different tune, or cease playing entirely, some adjustments must be made. These vary from unnoticed to complete breakdown, depending on the function and relative position of the affected cells. It is not the same if a third violin breaks a string or if the soloist breaks a string, though to the untrained eye they both look like violin players. Furthermore, no two soloists would react in the same way. One might snatch the first violin's instrument and continue without interruption, another might indicate for the orchestra to continue, or to start again, and the occasional *prima donna* would abandon the stage and leave the piece unfinished. All these reactions would have varying effects on the whole performance, but determinism is out of its depth here.

The function and reaction of every cell can affect the function of every other cell in the body, to a greater or lesser extent. A stimulus may have no noticeable effect, but it may also push the whole chaotic set-up around a new attractor. We may have to accept that many illnesses are not due to physico-chemical alterations, but to modified responses to information, so that we may never be able to predict illness and health precisely; not through lack of accurate instruments or measuring devices, but because of an essential uncertainty in the nature of the informational response.

As organisms become more complex and specialized, the response is more difficult to predict. From the cellular to the organ systems, to the complete organism, to social interaction, and finally linguistic interaction, we are faced with progressive increase in uncertainty of response. Statistics may be as close as we get.

Inorganic:
CAUSE → EFFECT

Organic:
STIMULUS → INTERPRETATION → PROBABLE RESPONSE
→ ALTERNATIVES?
→ NO RESPONSE

It is not the cause that determines the response, but the interpretation; that is what differentiates the chemical from the biological causality.

In the long run a deterministic science is apt to be as frustrating as it is expensive, but if we are prepared to approach biology and medicine from an informational point of view, we may find a whole new region to explore.

To even begin to understand about these complex functions, we need to learn a complete new language, the language of cellular and intracellular communications, of which we now are able to recognize only a few letters, perhaps a short phrase. The vast majority of the chemical and electrical markers a cell, an organ and a body use to coordinate and communicate, and the systems for interpreting these at different levels, are still entirely unknown. Perhaps the linguistic metaphor comes the closest, with molecules as letters and words, presented by some 'grammatical' structure for interpretation. Is it the molecule itself, its three dimensional structure, its concentration gradient, the alteration it induces in the membrane potential, or its association with other molecules which carries the message? Perhaps a combination of all these? The cell membrane, while carefully separating the cell contents from its surroundings, selectively permits entry to specific molecules with which it samples its immediate environment, that under certain conditions the cell may respond to, and which may affect its differentiation, growth and productivity. This is done much as the same way as we ourselves sample our physical environment with our sense organs and respond with our interpretation of this information. (Curiously, the sense organs and nervous system originate from the ectoderm in the embryo, the covering membrane.)

From a practical point of view, this concept need not radically alter either the practice of medicine, or the biomedical research. In most cases, we will be able to identify and associate a common response to a similar stimulus, and we may often be able to prevent an undesirable response by eliminating or altering the stimulus. We should however not be surprised when on occasions there is an alternative interpretation and then the response is not as expected; not through an error in the method, but because of the uncertainty built into the systems. As the organism becomes more complex, its possibilities of response increase, and the results are less constant. By the time we reach linguistic responses, which are entirely abstract and not even anchored to basic biochemical function, the possible interpretation of any particular stimulus are rather varied, and no one will ever respond with the exact words we expect to hear. The interpretation here may lead to alternative responses with, on occasions, undesirable results.

Research should be aimed to achieve a greater understanding of the interpreting mechanisms, with the understanding that they are interpretations which are by their very nature not entirely predictable. We may have to conform to uncovering the common associations and frequent responses, without demanding the absolute causality that would allow us a perfect predictability and a confident manipulation of biological organisms. Nature will always keep us guessing and uncertain, which is, when we come to think of it, part of her charm.