

RES MEDICA

Journal of the Royal Medical Society



The Design of the Organism

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Abstract

— being part of an address given to the Society on 15th November, 1963

Medical students and clinicians prefer — for different but equally good and acceptable reasons — to be presented with simple and easily comprehensible explanations of physiological and biochemical phenomena. But, as I have been saying to my students for years, the body was not designed for the convenience of the medical student or the clinician, if, indeed, it can be regarded as having been designed at all.

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ISSN: 2051-7580 (Online) ISSN: 0482-3206 (Print)

Res Medica is published by the Royal Medical Society, 5/5 Bristo Square, Edinburgh, EH8 9AL

Res Medica, Spring 1964, 4(2): 7-9

doi: [10.2218/resmedica.v4i2.417](https://doi.org/10.2218/resmedica.v4i2.417)

THE DESIGN OF THE ORGANISM

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Medical students and clinicians prefer — for different but equally good and acceptable reasons — to be presented with simple and easily comprehensible explanations of physiological and biochemical phenomena. But, as I have been saying to my students for years, the body was not designed for the convenience of the medical student or the clinician, if, indeed, it can be regarded as having been designed at all.

The popular notion of what it was designed for is that every discernible aspect of its functioning is there for the benefit of the organism, and it is a popular minor intellectual sport to 'explain' a physiological observation in terms of what you would have put it there to do. The exponents of this sport rarely, if ever, pause to think what happens when man designs a complex piece of machinery. When a team of able experts designs an aeroplane they can be moderately certain of a few things: it will fly: its speed will be in the expected region: its range will be much as hoped. But it is so complex that the inter-actions between many of its parts and functions are unpredictable. So the machine that is built to the design is put into the hands of a large team of other experts who spend years measuring hundreds of its properties in flight, and it will undergo successive small modifications intended to nullify the undesirable features that are disclosed by this study. When all this has been done with enormous care, industry and intelligence, it is still possible to leave the machine in possession of some such disastrous property as the unsuspected susceptibility to fatigue of the air-frame of the Comet.

Personally, I am firmly opposed to viewing the body as 'designed'. Quite apart from the dangers inherent in the easy superficial explanations of functions to which such a view inevitably leads, it leaves out two matters of importance.

In the first place, by satisfying one that everything is there, in the most subtle and intricate collaboration, to maintain the status quo, it makes it very difficult to understand the occurrence of any but the most gross of pathological processes. In the second place, it involves ignoring the conclusions of basic biology.

Biologists in general accept the notion of evolution by natural selection. By the nature of things, they cannot prove how evolution has occurred. But they have been able to observe it in action in some instances, and the biological phenomena which could form its basis are beyond dispute.

For instance, it is beyond dispute that errors occur in the duplication of chromosomes and that chromosomes can segregate during cell division in irregular fashions, so that parts of two chromosomes can interchange, or fragments can break off and be lost, or more than the normal complement of chromosomes can appear in a germ cell. Chromosome abnormalities in man in association with structural and functional abnormalities are now frequently being reported as the result of recent advances in the technique of study of chromosomes.

We can lump together all the random abnormalities of chromosome reproduction as mutations and we can call the bearer of such an abnormality a mutant. The theory of natural selection suggests that evolution is due to the survival of a mutant form because it possesses greater ability to adapt to its environment than does the original form, the 'wild' type.

Before we can understand the application of this notion, two points have to be taken into account. First, in a sexually reproducing organism, it does not seem likely that a single error, resulting in a unique mutant, could have much success in originating a new species. But it is known that particular mutations occur naturally with quite a high frequency, that is,

a particular kind of cell is prone to particular kinds of reproductive inexactitude. For instance, before modern haematological advances made life supportable for the haemophilic, that is before he had any significant chance of surviving to the reproductive age, new cases turned up with regularity, and it was clear that the mutation regularly occurred spontaneously. So, with a mutant form that does not confer a reproductive disadvantage, it is to be expected that it will accumulate in a population much more rapidly than if it had to rely for its spread on the progeny of a single mutant.

The second point is a more important one. Modern evolutionary studies have indicated that successful new forms are most likely to arise on the fringe of the habitat of the wild type. The fringe of the habitat is the region which is disadvantageous to the wild type, but just not sufficiently so to exclude it. The new form, then, does not have to be better adapted to the conditions of the major part of the habitat, but does have to be better adapted to the special features of the fringe area.

The consequences of this can be seen if some special instances are considered. An anaerobic bacterium, incapable of tolerating more than a trace of oxygen, can live in the deep layers of the soil. A mutant form capable of tolerating higher oxygen concentrations or of living fully aerobically could arise at the upper fringe of this habitat and could invade the upper layers of the soil. There is no reason why a second mutant could not arise from this one capable of tolerating lower oxygen concentrations, so that it could re-invade the original habitat. If it were incidentally more capable of tolerating the particular conditions of acidity of the lower soil than the original form it could compete with it successfully.

Two important considerations arise from this example: first, that successive mutations do not necessarily mean successive refinements of adaptations to one environment and, second, that since it is more likely than not that successive mutations will be at different sites, the double mutation will retain the properties conferred by the first mutation, even though they have no specific value in the new environment. Remember, in this context, that evolutionary success does not mean that the successful form is perfectly adapted to its environment. It merely means that it is better adapted than is any contemporary competitor for that biological niche.

This implies that complex organisms must

be expected to possess numerous features that were introduced a long time ago in evolution which have never disappeared because the pressure of selection against them has either never occurred or has never been strong enough. Recapitulation in ontogeny is sufficient evidence that this sort of thing occurs, but we rather tend to suppose that this is merely an anatomical matter, and we take comfort from such facts as that the pronephros and the mesonephros disappear during development, and that we are left with a respectable modern metanephros to look after our excretory needs.

But I think that we take comfort too easily, and that we are not really knowledgeable enough to be able to say how far cellular architecture conforms to an efficient pattern and how far it is cluttered with lumber from the evolutionary past. It is certainly true that there are anaerobic micro-organisms which contain cytochrome oxidase for which they cannot be seen to have a use and that there are marine worms containing a kind of haemoglobin which holds oxygen with such tenacity that the tension at which it will give it up is too low to support the life of the organism. Plants manufacture alkaloids for which no biological function can be found, and the form of the Peppered Moth which is now commonest all over England is so conspicuous in its black livery against the bark of clean trees, on which it rests with open wings, that it is an easy prey to birds. This last instance is particularly striking, because 60 years ago the common form was a pale speckled creature which is quite inconspicuous in this situation.

I believe that these considerations imply that the functioning of living organisms is based on crude basic mechanisms which have been overlaid from time to time by accretions, many of which are no longer particularly useful, which have tended to moderate the imperfections of the basic mechanisms in particular ways. Such arrangements might be expected to breakdown when stressed quite trivially in particular ways, and I believe that we could be better occupied in endeavouring to study the properties of these conglomerations than in searching for broad principles of design.

Have you ever thought of skeletal muscle as a kind of Heath Robinson contraption? Muscle cells at rest have rather a low oxygen consumption. As soon as the cells are stimulated to contractile activity the oxygen requirements rises enormously, and the cells are so constituted that oxygen lack or lack of a substitute

source of energy puts them rapidly into a state of contracture comparable with rigor mortis.

Yet, as soon as a group of muscle cells contracts, it exerts on the blood vessels running within it a pressure sufficient to occlude the blood supply: a process equivalent to putting a plastic bag over your head before you run for the bus.

The first stage adjunct to the muscular apparatus which offsets this major defect in design is the provision of a glycolytic mechanism. This enables the muscle to obtain some energy from the breakdown of carbohydrate to lactic acid without need for oxygen. But since the blood that brings oxygen also brings glucose, this mechanism is of little use without another, the mechanism of glycogen storage and breakdown.

The combination of these two adjuncts is of limited use: muscle cannot store much glycogen, and the glycolytic breakdown of carbohydrate provides only a fifth or a sixth of the energy that can be obtained by oxidation, so that the store lasts only a short time. In addition, the lactic acid formed in glycolysis makes the muscle more acid than usual and militates against function. So, even with these aids, the inherently bad design of muscle makes it difficult to maintain tonic activity or long-term phasic activity, as in walking or flight, for any length of time. With these mechanisms, we still do not have an effective basis for rapid flight from an enemy, on the ground or in the air.

However, a third supplementary mechanism exists. This is the provision of myoglobin. Myoglobin is closely related to haemoglobin in function, but it occurs in the muscle cells themselves. Whereas haemoglobin consists of four peptide chains, each of which is combined with a haem molecule which is responsible for the capacity of the haemoglobin to bind a molecule of oxygen, myoglobin consists of one such peptide chain combined with one molecule of haem. There seems to be no clear relation between the sequence of amino-acids in the haemoglobin peptides and that in myoglobin. The two haem-proteins appear to have arisen separately in evolution.

Myoglobin will still retain its complement of oxygen when the oxygen tension is much below that in arterial blood, but it gives up the oxygen at a tension which is still high enough to be of use intracellularly. Thus it holds on to oxygen inside the cell until the supply from outside has run out and then pro-

longs the period during which the muscle cell can function aerobically. It does for the muscle cell what the Chancellor of the Exchequer wishes that he could do for the economy: it irons out the swings in the relation between supply and demand.

You will note that this arrangement is not aiding the glycolytic mechanism. It is as though someone had thought that though glycolysis was quite a good notion for a beginner, it wasn't really good enough, and it would be better to try to solve the problem another way. The interesting thing is that the myoglobin mechanism is not only of a different kind from the glycolysis mechanism but it has quite a different incidence.

Whereas all skeletal muscle appears to possess the capacity for glycolysis and for the storage of glycogen, only certain muscles in certain species possess myoglobin. Think of the white meat and the dark meat: the pectoral muscles of the almost earth-bound domestic fowl have little or no myoglobin: those of the game birds, pheasant, grouse and partridge, for instance, are richly endowed with it.

Thus we can anatomize the apparatus for the provision of energy in muscle into elements which are independent, elements which are not inevitably brought together in every case, elements which fall into classes of basically functional and of superadded elements which serve to moderate the imperfections of the basic apparatus in fashions which are sometimes co-operative but sometimes independent.

Note that if cellular organisation is of this kind, then there is a strong probability that the superadded elements will introduce properties that are disadvantageous in some conditions, and keep in mind at all times that unless you are prepared to take the position that evolution is over and that neither man nor any animal whose physiology has been thoroughly studied is susceptible to modification capable of adapting the organism more fully to its present environment or to any environment at the fringe of its habitat, then you must conclude that in some context or other the organism has imperfections.

The simple explanations that we all need to enable us to focus on physiology are only a beginning of our study. If we accept these neat notions as true physiology then we are accepting a picture of man as man would have designed him had he had the forethought, and, at that, this is a picture of a design that has not been test-flown.