RES MEDICA
Journal of the Royal Medical Society

The Biological Basis of Individuality

M. F. A. Woodruff
M.D. (Melbourne). M.S., F.R.C.S.
Professor of Surgical Science, University of Edinburgh

Abstract

Philosophers have had much to say on the question of personal identity, though I must confess that I have not found any of it very helpful. Most of you, I suspect, would find yourselves in agreement with John Locke whose robust common sense has I think a special appeal to medical men, perhaps because he was one himself-that we each have an intuitive knowledge of our own existence. Some of you, on the other hand, as good sons of Edinburgh, may prefer the sophism of David Hume, and affirm that man is nothing but a bundle of perceptions-though Hume himself later in life appeared to have doubts about this. Perhaps, though I hope not, a few of you may believe that Society or The State is the smallest unit worth bothering about, and that what we call an individual is merely an abstraction.

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, Summer 1960, 2(2): 36-39
doi: doi:10.2218/resmedica.v2i2.341

THE BIOLOGICAL BASIS OF INDIVIDUALITY

By M. F. A. WOODRUFF
M.D.(Melbourne), M.S., F.R.C.S.
Professor of Surgical Science, University of Edinburgh

Based on an Address delivered to the Royal Medical Society on 23rd January 1959.

Philosophers have had much to say on the question of personal identity, though I must confess that I have not found any of it very helpful. Most of you, I suspect, would find yourselves in agreement with John Locke—whose robust common sense has I think a special appeal to medical men, perhaps because he was one himself—that we each have an intuitive knowledge of our own existence. Some of you, on the other hand, as good sons of Edinburgh, may prefer the sophism of David Hume, and affirm that man is nothing but a bundle of perceptions—though Hume himself later in life appeared to have doubts about this. Perhaps, though I hope not, a few of you may believe that Society or The State is the smallest unit worth bothering about, and that what we call an individual is merely an abstraction.

I am going to start with the common-sense assertion that all the higher animal species including man are made up of individuals, and that each individual is unique. Whether this holds good for lowly organisms such as bacteria I don't know, but for our present purpose it does not matter.

I am going to take it for granted also that the characteristics which distinguish different individuals are partly inherited, and partly the result of differences in environment.

You all know that the various tissues of the body are composed of cells and intercellular substance, and the question I want to discuss may be stated thus: To what extent are animal cells characteristic of the individual from whom they are derived? To put the matter another way: Mr Smith and Mrs Jones are different people, but is there something about an epidermal cell, a fibroblast or a chondrocyte from Mr Smith which distinguishes it from a cell of the same histological type from Mrs Jones? If so what form do these self-markers, as we may call them, take, and how can they be demonstrated?

There are two main approaches to this problem, which I shall call the **genetic approach** and the **immunological approach,** and these are becoming integrated in the newly emerging scientific discipline known as **immunogenetics.**

The basic concept of classical genetics, which dates from the time of Mendel, is the genetic factor or gene, which is a unit of inheritance often occurring in two or more forms each with a characteristic developmental effect. During the second decade of this century it was established that genes are carried in chromosomes and are arranged linearly, and following this a good deal of progress was made in the direction of correlating genetic and cytological observations.

The chemical composition of chromosomes was investigated and they were shown to be made up of desoxyribonucleic acid (DNA for short) and

protein, combined in a way that is still not completely understood. For many years it was believed that genetic specificity was determined solely by the structure and configuration of the proteins, but the demonstration in 1944 that transformation in type specificity of pneumococci could be brought about by highly purified preparations of DNA suggested that this substance might be the carrier of genetic information. A considerable weight of evidence in support of this hypothesis has now been accumulated, though in some plant viruses ribonucleic acid (RNA) appears to be the primary genetic material.

The DNA protein, according to one view, assumes the configuration of a double helix of two complementary polynucleotide chains which are capable of replication, and in which the genetic information is coded in the form of specific sequences of purine and pyrimidine bases. Gene function depends on the translation of DNA specificity into protein specificity, probably via an RNA template mechanism.

As you know changes occur in genetic coding as a result of a variety of processes—gene mutation, crossing over, and others of a more esoteric kind, and the question of controlling such changes constitutes a challenge for biologists comparable to those of nuclear physics for its devotees.

One method which has been used extensively is exposure to ionizing radiation, but it is a crude sort of procedure—just as radiotherapy and, for that matter, surgery are crude procedures, which in time will I think be largely replaced by more elegant methods of treatment.

Another approach arises out of the observation that genetic transformation in bacteria can be brought about by exposure to free DNA, or by the action of bacteriophage particles which carry genetic material from one bacterial cell to another in a manner which to the non-bacteriologist (and I might add non-apiarist) suggests the thought of bees carrying pollen from one flower to another. Can the same sort of thing be done with the germ cells of higher animals? You will remember that in 1957 Benoit and his colleagues in Paris said that it could in ducks. Most geneticists however have been publicly sceptical about this—one at least published some stern criticism in *The Scotsman*—but if you wander round the world you will find that a lot of experiments of the same sort are being conducted, and one has the feeling that some geneticists at least protest too much.

The standard genetic test for detecting changes in genetic coding in the germ cells of an individual is to study the characteristics of offspring one of whose parents is the individual in question. The choice of the other parent, and of the characters to be studied, depends on many factors which we need not consider here; the point I want to make is that the test is of decidedly limited application.

A more direct approach would be to try to demonstrate differences between the cells of different individuals. In theory this might be done chemically or cytologically, but in practice, as far as differences between individuals which are members of the same species are concerned, these methods do not take us very far. The chemical attack on the problem has begun with the recognition that there are several different human haemoglobin molecules, but the chances of distinguishing at present by this test between two people picked at random are extremely small. Similarly, cytological observations, though they enable us in some species to determine whether an epidermal cell or a polymorphonuclear leucocyte is from a male or female individual, and occasionally to recognize cells from members of an inbred strain by means of a characteristic chromosomal marker, are quite inadequate for our purpose of distinguishing routinely between randomly

chosen individuals. There remains the immunological approach, and I want to consider this in a little detail.

The basic method of investigation is transplantation, and this simple procedure has yielded results of quite remarkable importance. Let us look at the basic facts. If you take a piece of tissue and transplant it autologously, i.e. from one part of the body to another place in the same individual then as a general rule, if its nutritional needs are met, it will survive permanently in a new enviroment. A familiar example is that afforded by the skin grafts which are used in treating burns and for many other purposes in reconstructive surgery. If, on the other hand, the tissue is transplanted homologously, i.e. to another member of the same species, it typically survives for a time ranging from a few days to a few weeks, but sooner or later becomes invaded by cells of the recipient and is destroyed.

There are exceptions to this; for example transplants exchanged between identical twins behave like autologous transplants, and homologous transplants of cornea may survive indefinitely, probably on account of their avascularity, but the rule holds good in a very wide range of cases.

It was shown by Gibson and Medawar, and has since been confirmed by hundreds of investigators, that a second transplant from a given donor to the same recipient is destroyed more rapidly than the first. This suggests that the destruction of homologous transplants is an immunological phenomenon, and confirmation has been provided by the discovery of Mitchison that the state of increased resistance to transplants from a given donor can be transferred "adoptively" to a third member of the same species.

A good deal is now known about the antigens responsible for immunity to homologous transplants. It was thought first that they were DNA protein, like the units of genetic inheritance, but it now appears that they are complex polysaccharides which are normally carried on DNA protein molecules. They are determined genetically by a particular class of genes known as histocompatibility genes. Linkage has now been demonstrated in mice between histocompatibility genes and genes responsible for a variety of somatic characteristics, and this discovery forms the starting point for the new and rapidly developing science of immunogenetics.

The search for antibodies in the serum of recipients of homologous transplants has proved less rewarding. There is abundant evidence that the cells of the recipient play an essential role in the destruction of such transplants, and even when humoral antibodies can be demonstrated it often remains doubtful whether they play any part in the destructive process.

It is natural to ask why, if what has been said is correct, the mammalian foetus, part of whose genetic inheritance is derived from the father, is not treated by the mother as a homologous transplant and destroyed. It has been shown that there are several factors which help to prevent this catastrophe, the most important being the existence of a barrier in the placenta which normally prevents maternal cells from entering the foetal circulation and vice versa. It is known that if this barrier breaks down in humans the mother may become sensitized to certain blood group antigens of the foetus and that haemolytic disease of the foetus may result, and it seems quite likely that much unexplained foetal morbidity and mortality may also turn out to be due to maternal immunization resulting from placental leaks.

A more subtle question was propounded by Sir MacFarlane Burnet who asked why the immunologically reactive cells of an individual do not react against all the tissues which make up his body. The discovery that some diseases are in fact due to "auto-immunization" adds point to Burnet's

question. By way of answer Burnet, and his colleague Fenner, postulated that all the cells of an individual carry a series of self-markers which his immunologically active cells learn to recognize, and they predicted that if an organism at an early stage of its development received an injection of cells from another individual, then, when it grew up, it would permanently accept transplants from the cell donor. Burnet has since modified his hypothesis, but his prediction has been shown to be true. The "injection" of cells may be performed experimentally; in addition in cattle, and very occasionally in other species including man, cells may be transferred between twins *in utero*, and when this happens even non-identical twins will subsequently permanently accept transplants from each other. Individuals who carry permanently in their bodies cells derived from another individual are known as chimeras, and are said to display specific immunological tolerance towards the foreign cells.

The upshot of all this is that it is possible to distinguish by transplantation the cells of any individual from those of all others even of the same species, except only when the individuals concerned are (*a*) identical twins, (*b*) members of a strain of animals which has been maintained by brother x sister mating for so long that it is genetically virtually uniform, and (*c*) non-identical twins which happen to be chimeras.

There appears the exciting possibility that in producing chimeras we may learn how to introduce characters which are hereditarily transmissible, and so achieve even in mammals a sort of biological transmutation comparable to the transmutation of elements achieved by nuclear physics.

The surgical implications of the phenomena we have been considering are to me no less exciting, but this is another story and one which I must leave for another occasion.