REITH LECTURES 1991: The Language of the Genes

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Lecture 1: A Message from our Ancestors

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If you visit Sigmund Freud's house in Hampstead, you see on his desk some unexpected objects - a stone axe, an Egyptian scarab and some ancient figurines. These, he suggested, were relics of the childhood of the human race; messages from our ancestors, whose experiences in the dawn of humanity still shape our lives. The guilt of those in the dim past, who killed their father for raping the women of their tribe, lingers on today; and, according to Freud, many of our anxieties and our neuroses are a memory of ancient times which can only be uncovered on the analyst's couch.

Our genes, too, are messages from the past - and much more reliable than those received by Freud. Only in the past 20 years have we begun to read the language of the genes, to decipher our own instruction manual and understand the clues about ourselves left by our ancestors. In these lectures I will ask what genetics can - and, more important, what it cannot - tell us about the history, the present and the future of humankind.

The idea that the human condition can be explained by events that took place long ago is central to psychoanalysis, to religion and - for that matter - to much of politics. Recently, some psychologists and politicians, but not many geneticists, have claimed that we're controlled by messages from our ancestors. They promote a kind of biological fatalism: humanity is driven by its genes and our biology is a sort of original sin. The poor are victims of their genes; their predicament is due to their own weakness and has nothing to do with the rest of us. Such nouvelle Calvinism suggests that as human life was programmed long ago there is no point in trying to change it, which is convenient for those who like things the way they are.

Freudians, politicians and historians see almost no limit to what their pet theories can explain. Science, in contrast, is a strictly limited endeavour; the study of evolution perhaps most of all. It's the essence of any scientific theory that it cannot explain everything. Every scientist spends his time trying to disprove his own pet theories, to slay his intellectual children, in contrast with those involved in other creative endeavours. Science can't answer all our questions - particularly the sorts of things that analysts - or children - ask. Why are we here? What is the point of being alive? How ought we to behave? It has nothing to say about such things; and almost nothing to say about what makes us more than just machines driven by biology, about what makes us human.

In retrospect, much of human genetics before the war was scarcely a science at all. It was quite unwilling to accept its own limits. Soon after it began, human genetics found itself - somewhat to its surprise and almost uniquely among the sciences - being asked for advice about good and evil, the quality of people, and the kind of society we should live in. Some geneticists felt that they were qualified to comment on such issues. Sometimes, they were even taken seriously, with disastrous results.

This history has made those in the field today very cautious about claims that the essence of humanity lies in our genes. Modern genetics is one of the few sciences which has reduced its expectations. It has certainly shown why sociology is best left to sociologists and politics to politicians. But the new genetics - together with an older theory, the theory of evolution - has also given us a unique and startling insight about where we came from, how we filled the world, and what sex, age and death really mean.

Darwin, like Freud, saw the past as the key to the present. He proved that the pattern of life in modern creatures shows how they are related to each other, what their ancestors were like and how life progressed from its beginnings to the present day. The most famous line in The Origin of Species is that "light may be shed on man and his origins". Darwin's hint that humans share a common descent with every other creature is now accepted by all biologists - even if it is not by nearly half the American public. His hint about our ancestry has been more than confirmed by modern biology. Our understanding about our place in nature has been transformed by the new ability to read the inherited messages from the past.

Before genetics - indeed, even 20 years ago - we knew almost nothing about our own beginnings. Written history does not start until two hundred or so human generations ago. Myths go back a little further and often seem to be trying to tell us something about our origins: a hero's descent into the underworld and safe return is in the Bible, the Odyssey; and the Epic of Gilgamesh, current about 5,000 years ago. Gilgamesh had a Garden of Eden and a flood. If you add up the generations listed in the Bible to estimate the date of Noah's Flood, you get a date of 2349 BC. New geological evidence shows that there was a flood in the Middle East about then. The myths preserve some hints of the truth.

Fossils, too, are hints about the past - and often, not much more than that. Even in the best fossil beds, fragments of only about one individual in ten million are preserved. Not surprisingly, there are still furious arguments among palaeontologists about where humans first arose and how they filled the world. Their main problem is that we can never be sure that any fossil has left a descendant alive today.

In contrast, we know that every one of our genes must have an ancestor. We can use them to piece together a picture of human history more complete than from any other source. Each gene is a message from our past, and together they contain the whole story of human evolution. Genes give us a better insight about who we are than anything else. Each one of us is a living fossil, carrying within our genes a history which goes back to the beginnings of humanity and far beyond.

The historical documents are of many kinds. Some are easy to read. A few families make a point of preserving their ancestral messages. As we will see, royal families play an important part in genetics - why we can understand when we consider that one enthusiast has traced 262,142 alleged ancestors of Prince Charles. The aristocracy were the first geneticists, interested in shared descent. They often kept detailed pedigrees. The family Temple-Nugent-Bridges-Chandos-Grenville has a mere five multi-barrelled names - but it has 719 symbols on its coat of arms, each showing a genetic link to another line of inheritance.

Names and arms often travel down the generations in consort with genes. The Habsburg name and its crest - a hawk - lived through 700 years of European royalty. Those inheriting these were liable to get something else: a gene for a protruding lower jaw - the Habsburg lip. The famous lip can clearly be seen in the Holy Roman Emperor in 1450, and was still prominent in the Spanish royal family a century ago. This particular gene does not do much more than confirm what we know about ancestry from the records of one family. Every family, aristocratic or not, inherits a genetic record. Sometimes errors in the message, genetic abnormalities, are the only clues of shared descent. A form of juvenile blindness - hereditary glaucoma - is found in France. Painstaking searches of parish records show that more than half the cases are descended from a single couple who lived in a village near Calais in the 15th century. Even today, pilgrims pray in the village church, which contains a cistern whose waters are believed to cure blindness. Thirty thousand descendents of this couple have been traced; and, for many, the diagnosis of the disease was the first clue about where their ancestors came from.

Today's Britons trace their ancestry from many parts of the world; from populations with black skin or white, round eyes or narrow. These characters are certainly some clue as to where their families came from; but a very incomplete one. Fewer than 10 genes are responsible for the difference between the blackest and the whitest human skin. What we need are more inherited messages. Fortunately, modern genetics gives us just that; clues about our evolutionary past which take us back to the beginning of humanity 100,000 years ago and to the origin of life 3,000 million years before that. These clues can be read as a language. Genes and languages evolve in much the same way. Genetics is a language, a set of instructions passed from generation to generation. It has a vocabulary - the genes themselves; a grammar - the way in which the inherited information is arranged; and a literature - the thousands of instructions needed to make a human being. The language is based on the DNA molecule, the famous double helix; the icon of the 20th century. It has a simple alphabet; not 26 letters, but just four, the four different DNA bases - A, G, C and T for short. These are arranged in words of three letters such as CGA or TGG. Most of the words code for different amino acids, the building blocks of the body.

Just how economical this language is, I can illustrate with a rather odd quotation from a book called Gadsby, written in 1939 by one Ernest Wright: "I am going to show you how a bunch of bright, young folks did find a champion; a man with boys and girls of his own; a man of so dominating and happy individuality that youth was drawn to him as a fly to a sugar bowl". This sounds rather peculiar, as does the rest of the 50,000 word book, and it is. The quotation, and the whole book, does not contain the letter E. We can manage to write a meaningful sentence with 25 letters instead of 26, but only just. Life manages with just four.

Although the DNA message is simple, it is very long. Each cell in our body contains about six feet of DNA. A useless but amusing fact is that if all the DNA in all the cells in a single body was stretched out, it would reach to the moon and back 8,000 times. There is now a plan to read the whole of its 3,000 million letters and to publish what may be the most boring book ever written; the equivalent of around a dozen copies of the collected works of Sigmund Freud - which itself fills 24 solid volumes.

There is much disagreement about how to set about reading the message, and even about whether it is worth doing at all. It probably is: the Admiralty sent the Beagle to South America with Charles Darwin on board not because they were interested in evolution but because they knew that the first step to understanding - and, with luck, controlling - the world was to make a map of it. The same may be true of the genetic map of ourselves. To make it will be expensive - in fact about the cost of a single Trident submarine. The task will also be a stupefyingly tedious one for those who actually have to do the work.

It's been suggested, not wholly in jest, that molecular biologists found guilty of faking their results should be sentenced to sequence 1,000, 10,000 or 100,000 DNA letters depending on the gravity of their crime.

One of the first discoveries of the geneticists who set out to make the map of ourselves was that we are all different; far more different than anyone had previously thought. There are now thousands of inherited clues - perfectly normal variation, not diseases - which can be used to look at patterns of shared ancestry. Because all modern genes are copies of genes from our ancestors, the differences between people can all be used as messages from the past.

Obviously, people look different one from the other. But what we can see is just the tip of the iceberg of human uniqueness. Even a trivial test shows some hidden inherited differences. Stick your tongue out. Can you roll it into a tube? About half the British population can, and half cannot. Clasp your hands together. Which thumb is on top? Again, about half the population folds the left thumb above the right and about half does it the other way. These characteristics certainly run in families, but the details of their inheritance - like the inheritance of the way we look - are a bit of a mess. Some individual differences are under simpler genetic control.

In the 1930s, a manufacturer of ice trays was surprised to receive complaints from his customers, who claimed that their ice tasted bitter. This baffled the unfortunate entrepreneur as the ice tasted just like ice to him. It turned out that there are genetic differences in the ability to taste a chemical, PTC, used in the manufacturing process. To some, a trace of this chemical is intolerably bitter, while to others a concentration a thousand times greater has no taste at all. The difference depends on just one gene which exists in two forms - taster and non-taster. When I was a student it was regarded as superbly witty to make tea containing PTC and to observe the bafflement of those who could drink it and those who could not. Now, unfortunately, students have more sense.

There is a lot more variation than this rather silly example. When blood from two people is mixed, it may turn into a sticky mess - which would be fatal in a blood transfusion. The process is controlled by a system of inherited clues on its cells - the blood groups. Only certain combinations can be mixed successfully. There are plenty of different blood group systems - some familiar, like ABO and Rhesus; others less so, like Duffy and Kell. Millions of people have had them tested. A dozen systems are routinely screened; each with a number of different forms. A large amount of diversity is generated by just this small sample of our genes. The chances of two randomly chosen Englishmen having the same combination of all 12 blood groups is only about one in 3,000.

Blood groups were discovered in what we now regard as the Stone Age of molecular biology. Since then, there has been a technical revolution. Like the neolithic revolution, which gave rise to modern humans, this depends on some simple tools which can be used in many different ways. We can now decipher the actual order of letters in the genetic message.

What happens when we compare the DNA of unrelated people in this way? It turns out that - just as in blood groups - everyone, except for twins, is different. On the average, two people differ in about one DNA letter per thousand. This gives about three million places in the inherited message which differ from person to person. Our personal uniqueness itself tells us something useful about ourselves. Molecular biology has made individuals of us all. Nobody who ever has lived, or ever will live, is built on precisely the same genetic plan as anyone else. This information helps us to understand where we fit in the family of humankind and in the living world as a whole.

Relatives are more likely to share genes than are unrelated people because of course they have an ancestor in common. This means that we can use genes to test family relationships; the more genes two people share, the more likely they are to be related. Exactly the same logic can be used to sort out more distant patterns of relatedness - even, as we will see, the shared ancestry of humans and other creatures.
This is very easy when close relatives are involved. Before DNA tests were available, immigration officers often refused to believe that a particular child was the offspring of the woman who claimed it. The tests nearly always showed that the mother was telling the truth.

Shared genes allow us to search out more distant relatives, too. During the military dictatorship in Argentina, more than 10,000 people disappeared. Most were murdered; some of these were pregnant women who were killed after they had given birth. Many of the children born were stolen by military families. After 1983, a group of mothers of the murdered women began to search for their grandchildren. American scientists set out to compare the DNA of these children with those who claimed to be their grandparents. The message passed in the genes from grandparent to grandchild allowed more than 50 of the children to be restored to the biological families from those who stole them.

Our own personal combination of genes comes from ancestors who died long before our grandparents. It's in some ways a genetic coat of arms. And, like the shield of the Temple-Nugent-Bridges-Chandos-Grenvilles, it contains a record of who our ancestors were and who they were related to.

When people move, they take their genes with them, so that by making maps of genes in modern humankind we can do more than just trace descent; we can use genetics to recreate history.

Sometimes history itself is a clue as to where to start. Alex Haley, in his book Roots, used documents on the slave trade to try to find his African ancestors. He found only one, Kunta Kinte by name, who had been taken as a slave from the Gambia in 1767. The patterns of genetic diversity in today's black Americans could have told him much more. About 15 million Africans were shipped to the Americas. They came from all over West Africa and were dispersed over much of the New World. Slave owners had distinct preferences. In South Carolina, slaves from the Gambia were favoured over those from Biafra, as the latter were thought to be hard to control. In Virginia, the preference was in the opposite direction. We can now use genes to sort out just who went where and where they came from.

Many Africans have an abnormal form of the red pigment of the blood, haemoglobin. This "sickle-cell" form protects against malaria. The gene involved is associated with different DNA variants in various parts of Africa. Because of its medical importance, this DNA has been much studied. We could use the details of DNA structure to track down just where in Africa the ancestors of any US black person originated. Black Americans in Baltimore, in the north, have a different set of variants from those in the southern states because of the difference in the slave markets 200 years ago. Alex Haley, by comparing his genes with those from different African countries, might have learned much more about his ancestors than he could from the written records. Our genes have already taken us back for hundreds of years. But they bring messages from far longer ago. Some of these give surprisingly subtle hints about the patterns of life in ancient human society. They suggest, for example, that men and women have a different history which may stretch back to a time before the origin of agriculture.

Some genes are inherited mainly through females. All our cells contain mitochondria, small energy factories. These have their own tiny pieces of DNA, distinct from those in the cell nucleus where the great majority of genetic information is stored. Sperm contribute very few mitochondria when they fertilise an egg, so, like Jewishness, this DNA is passed through the female line. It contains the history of the world's women, with almost no male interference. For example, Queen Elizabeth II's mitochondrial DNA descends not from Queen Victoria, her ancestor through the male line, but from the less eminent Anne Caroline, who died in 1881.

The patterns of change in mitochondrial genes differ from those which pass down through both males and females. The way they behave is, by coincidence, rather like the evolution of first names. Boys' names don't change much from place to place in the English speaking world. Girls' names are more localised and evolve more quickly. Only one of the top ten girls' names - Sarah - is the same in the United States and in England. In contrast, five of the ten favourites among boys are the same on both sides of the Atlantic: Michael, Christopher, Matthew, Daniel and David. The distribution of mitochondrial genes is similar to that of girls names. Mitochondrial DNA - the female kind - is variable, and each type is quite localised. In African pygmies, shared mitochondrial types are rarely found more than about 20 kilometres apart. The genes carried by both sexes cover a much wider range - in the pygmies communities 500 kilometres apart are not very different in genes which pass through males as well as females. This may be a message from the distant past about the role of men and women in society. Men have ranged widely - perhaps through hunting, perhaps because of warfare - while women tended to stay at home.

The fossils show that our ancestors appeared in Africa about 100,000 years ago. We have other African relatives too. One of them, the chimpanzee, has always seemed particularly close to ourselves. So much so indeed that one chimp - Koko, an inhabitant of the Gombe Stream Reserve - was the first animal to have an obituary in the Times. Chimps share many of our genes. A distinguished and famously humourless geneticist of the 1940s once tested whether they share our variation in tasting the bitter chemical - PTC. He fed this stuff to three chimps at London Zoo. Two swallowed it, with every sign of delight; but the third spat the liquid all over the famous professor. This - unscientific though it is - at least suggests some genetic sharing and common ancestry of chimps and ourselves. We now know that this goes much further. One estimate is that we share 98 per cent of our genetic material with chimps. We can trace relatedness to the rest of the animal kingdom as well. It has been known for many years that mice and men have a lot in common. Scores of human genetic diseases are also found in mice. We share even more genes with rabbits. Whether we should be proud of this or not, I'm not sure.

To me, this new work on gene sharing in some ways puts paid to the whole idea that genetics can tell us anything about the human condition, about the nature of humanity. A chimp may share 98 per cent of its genes with us but it is certainly not 98 per cent human: it is not human at all. It's a chimp. And does the fact that we share some of our genes with a mouse - or a potato - tell us anything useful about ourselves? I have seen claims that the human DNA sequence will give us a new philosophical insight - that we will find the gene that makes us human. This idea seems to me ridiculous. Just how ridiculous it is we can see by looking at the search for another important gene - the gene that makes me male. This was tracked down a few months ago, and its message spelt out in the four DNA bases. It starts like this - GAT AGA GTG AAG CGA. There are about 240 of these letters in the whole message. I'll spare you from having to listen to the whole tedious story of being a man. This gene is all you need to attain the elevated status of masculinity. If it is inserted into a developing female mouse, then it turns into a male mouse. However, surely the dim little message I have just read does nothing to tell that half of the population - which is unfortunate enough not to have it - what it is really like to be a man rather than a woman. Masculinity means a lot more than a sequence of DNA bases. The same is true for humanity.

One of the problems of modern genetics is that it usually fails to live up to its headlines. My favourite, incidentally, was one in an American newspaper - the National Enquirer - which greeted the first study of fossil DNA as: 'US scientists clone dinosaurs to fight on after nuclear war'. Headline writers have to break a complicated story about human life into a message made up of a few letters. It is a natural mistake to think that the genetic message summarises information about ourselves in the same way. The error comes from overstating the successes of the scientific method.

Usually this is reductionist. To understand something, one has to break it down into its component parts. The approach certainly works well as far as it goes, but it only goes so far. Where it does not work, we can see in a phrase notorious in British politics: Mrs Thatcher's statement that "there is no society; there are only individuals". The failures of this philosophy are all around us. To say there are no people, there are only genes, is to fall into the same trap.

Human genetics has been transformed in the past 50 years. Geneticists too have had a change in attitude. Fifty and more years ago, some geneticists were filled with extraordinary self-assurance. They were happy to make sweeping statements about the importance of genes in helping humanity to understand itself; and about their relevance in shaping society or even politics.

As is often the case in science, knowledge is accompanied by humility; the more we know, the more it seems that there is to know. Geneticists nowadays have no interest in what their subject might say about the large and vague issues which occupied their predecessors. Instead, they concern themselves with purely scientific questions, or with helping those who suffer from genetic disease. Genetics has matured as a science; it sees its own limitations.

Genetics certainly can, like anatomy, sociology or psychoanalysis, give us a glimpse of some of the elements which together make up humanity. Freud’s own work tells us something about ourselves which genetics does not. He was wrong in thinking that events in the childhood of the human race persist in our subconscious today. But one thing is clear: in one sense - even if only one - Freud was right. We do have within ourselves a record of our earliest beginnings. Our genes have a memory, and at last we have a way of persuading them to recall the past. In the remaining lectures I will ask what the genes can tell us about human evolution, and will end with some guesses about our biological future.