Genetics

I'm very pleased to say, to welcome Professor Jones, Steve Jones, the Geneticist, UCL's leading geneticist and he will talk to you on that subject with reference to the Royal Family, our premium genetic pool. (Laughter) away you go.

Okay. Thank you for that I've been told I need to speak in a comprehensible way being a scientist will be very difficult if not impossible but I'll give it my best. I'm going to talk about nature and nurture, the degree to which what we are turns on our genes and on our DNA versus our environment and the way we live and that's actually a theme which is very close not only to genetics but to life in general. Most people are interested in whether they are born with any particular attributes and if they are born with it, perhaps it can be passed on to their offspring. The question of separating nature and nurture in human environment is actually a very difficult one. The idea goes back a very long way as fluent English speakers you will all of course have read Shakespeare's Play The Tempest and um in that famous play which is set on an Island, there is a devil who lives on the island called Caliban and Shakespeare was the first person to use that phrase nature and nurture. The Hero says to the devil (Caliban) "on thy foul nature, nurture will never stick" in other words you're so awful that nothing we can do will change you. And I want to explore that notion of inheritance, nature and nurture.

Now clearly all kinds of things are inherited. Here we have a slide, a picture of a fairly well known family and it's clear that at least one of the children has inherited a mild genetic disease of the ears, okay (laughter) and the other one hasn't. I never know which is which. And one of them has got it and the other hasn't and we know a lot strangely enough about the genetics of the ears and we know indeed that having your ears sticking out like that is pretty much controlled by a pattern in the DNA. So that's, that's inherited in its very nature but of course the other one may also inherit something from his father (possibly) which follows very strict rules and is passed on from generation to generation because he will inherit this (picture of the crown jewels) and theses you will of course recognise as being the crown jewels of Great Britain and the Commonwealth erm which are passed on and have been passed on for many hundreds of years from one sovereign to the next. But of course there is no gene for inheriting the crown jewels that's simply passed on because he happens to live in an environment called Buckingham Palace which he good to, is going to inherit from his father. So actually the fact that something is passed down generations doesn't necessarily mean that it's coded for in the DNA. However an awful lot of things are coded for in the DNA and DNA is extremely important. So lets look at that simple fact (slide of childhood survival in England) erm first of all lets go back to The Crown Jewels for a second.

Now let me introduce the idea that DNA is important by asking everyone of you to look at the person to your left and the person to your right OK I can assure you with a fair amount of confidence that two out of the three of you will die for reasons connected with your DNA with your genes erm which is a bit depressing but if you find it too depressing I could point out that had I been giving this lecture in London five Hundred years ago two out of three of you would be dead already. And of course in many parts of the world that figure would have been true much more recently. So here are the figures for England childhood survival of every million babies born in Britain how many survive to be twenty one. In sixteen hundred, just four hundred years ago, it was indeed only about one in three. In seventeen hundred, it was about a half by nineteen hundred only about three out of every four babies lasted until they got to be twenty one and in two thousand and one, ninety nine per cent of all babies born in England lasted until twenty one. Erm Now that's an astonishing shift of course, and of course it's a shift that's happened all over the world if we were to look at somewhere like China let's say erm I don't have the figures in front of me but the figures are exactly the same Chinese health, Chinese health care, Chinese mortality has shown a dramatic improvement over the last fifty or a hundred years. So clearly er changing the environment can make a great deal of difference to your survival however the reason that two out of three of you will die of a reason connected with your genes is that everybody of course dies in the end erm which is a cheery thought now our life expectancy in the west has been going up from an average of around fifty years to an average of around seventy five or eighty women lasting longer than men now but it might continue to go up slightly but its never going to be a hundred and fifty. So in the end you're going to die and the reasons you die come from within. We can see three great eras, three great periods in human history the first one and the longest one I sometimes think of as the age of disaster and that was ninety percent or more of our evolutionary history which began as modern humans about a hundred and fifty thousand years ago for ninety per cent of that time we lived by hunting and by gathering we lived in small groups who moved around the countryside picking fruits and vegetables killing animals and eating them ok. And actually life was pretty healthy there weren't many infectious diseases but people died. They died because they starved to death possibly there wasn't enough food or they were killed by a sabre toothed tiger or they died through violence, erm so that was the age where you died disastrously. About ten thousand years ago, there was the origin of farming and the only thing that happened more or less simultaneously through the Middle East and in China a little bit later in China, and a little later again in Northern and South America and that led to an extraordinary explosion in the numbers of people. We are now, given our body size and were

quite big mammals, we are now about ten thousand times more common than we were when we were hunter gatherers or than we ought to be given if were just ordinary animals erm the natural population of the world is only about one ten thousandth of what it is today. Well that's fine, we've got much more common that's entirely due to farming forty per cent of all the suns energy that falls on the earth now goes to feed human beings which is a frightening rather frightening statistic but it led to a new age of death which we can I think of as the Age of Disease because in order to get epidemic diseases you need to have dense populations lots and lots of people and its an interesting thought that those dense population are new, everyone of you on your way to UCL this morning saw more people than the average pre-farming human being would have seen in his or her lifetime. So now we are very very abundant and we move around a lot and of course diseases spread very rapidly. If we look at the great plagues like the Black Death um in Europe in the Middle Ages or Cholera in the Far East in the nineteenth century they all happen in dense populations so people died in large numbers of disease. But basically in most of the world outside Sub Sahara Africa and small parts of the rest of the world we've controlled most infectious diseases, people no longer die of the Black Death or Small pox or they do die of Malaria but that's an exception erm so we've controlled those diseases. So we have another age which we now live in, which has only really been here for about fifty years and that's the age of decay the age when everyone of us will die of a disease we can do nothing about which is old age and the great number of the diseases, illnesses of old age are affected by genes: diabetes: heart disease: cancer you name them they have a strong genetic component behind them. A great deal of the research here at UCL is actually based on trying to understand those diseases which are common and which will in the end, depressing though it is affect all of us in this room. So why do we do that research what is the point of understanding the genetics of disease of course surely if something is inherited its in the DNA there's nothing you can do about it. That I have to tell you is completely untrue er the more we learn about inherited disease the more the environment becomes important and that what I want to spend most of my time talking about is about DNA, what it is? and how it interacts with the circumstances in which I finds itself.

Well we all know what DNA is it's the famous double helix there a lot of it around, if anyone of you consumed by boredom at my talk was to rush out of their office building into Gower St lets say and you took a hit by a number twenty four bus and squashed flat. I mean very flat so that all the DNA in your body was squeezed out. The DNA in your individual body would stretch from that damp spot on the pavement to the moon and back eight thousand times. There are several million miles of DNA in your body um and that's because there are several million million cells in your body each of which contains about two metres of DNA. Well that DNA has been sequenced its of course built on this famous and very boring language which not everyone can understand because its only got four letters it's a great sequence of letters, there's only four of them, arranged in groups which code for amino acids which in turn code for the proteins of things that make us what we are. And the things to which we sum small that are left over for example in McDonald's hamburgers alright.

One of the big surprises of sequencing the DNA was to find that that first of all a lot of it seems to be junk seems not to have a job to do which is surprising which appears to be true and secondly that actually there are rather few genes that go to make a human being. When I was a student a long time ago and indeed until five years ago or so most people would have thought how many pieces does it take to make a human being? In the old days they used to say a million two, million. Then perhaps it was up to two hundred thousand half a million er in fact the real number of genes is amazingly small er lets go back to that bus that's just run you down actually it's a number eighteen not a number twenty four even though it doesn't go down Gower St. This bus here one of Kens, Red Kens not pale pink Kens um er bendy buses that's got about twenty five thousand different parts in it, plenty of screws: bolts: bits of electrical wiring: resisters: break pads er valves you add all the pieces together, you get about twenty five thousand of them. A human being and here's a human being with rather more arms that usual has got about the same number of parts. It takes about twenty five thousand genes to make a human being. Now I would like to think, perhaps wrongly that I am more complicated than a bendy bus but I'm not and neither are you or to put it another way. I think all we've done by unravelling and reading this DNA message is to realise how little we understand about genetics. What we've got is a big pile of buckets labelled bolts, screws, washers, valves and we don't understand how they all fit together so in fact perhaps we understand rather less than we thought about the actual Genome. The other interesting thing about the Genome is that, actually there's a huge amount of variation in it. There are three thousand million letters and about one in every thousand varies from person to person. So that means if you were to look at the person next to you as long as your not identical twins and, as it happens my mother is an identical twin, which is not why I became a geneticist. Er then you are different from them at about three million DNA sites and that means that you are unique , you are different from everybody in the room ,different from everybody in the world and different from everybody whoever has lived in the past or ever will live in the future. Simply because there's so much variety. And we know, a lot about the variety as far as we know doesn't do much. But it tells us a lot about who we are. It tells us, for example how we are very closely related to other creatures, we share about ninety nine per cent of our DNA even with Chimpanzees. Now many people don't believe that we evolved from a common ancestor with Chimpanzees. The evidence that we did is all around us. (Slide of Bush with Chimps - Laughter) This is my favourite slide, this could be used in all lectures erm and um it's clear that we have chimpanzees in our DNA, some of us, some of us more than others. So that's what genetics is so, so that's what genetics is and genetics without question is very, very important.

So I've talked a bit the depressing with a depressing tale about the illnesses of old age and we know about many of them um um: cancer, and diabetes coronary heart and the same. Many people don't realise that worldwide and I mean worldwide all over both the developed world and the developing world there is a severe epidemic which is underway which is likely to become the most dangerous killer of all and its this one (slide) Its obesity, Ok, obesity or being overweight, already and I don't know whether any you have being to the United States, already its very obvious if you go over there, half the population is clinically obese. They are grossly overweight er Britain we're proud or not proud to say is the fattest country

in Europe um and er although still well behind the United States and places like Indian now have this problem because the Indian diet is actually a very fattening diet when it's present in large quantities. And being overweight is very dangerous; it leads to all kinds of problems that we will see in a minute. Now clearly being overweight runs in families, here we have a picture taken of two American parents and their daughter ok and their daughter is overweight and many people who are obese say and perhaps they believe, that they are obese because of the way they were born, because of the genes that they carry. Well maybe and maybe not we'll have to look at it, but there is a rather interesting clue in this family as to what causes the problem for these people here. Here's a picture of their cat, (gasps) which as you can see is what's technically known as a fat cat. And its one of those remarkable and fascinating facts that people's pets are very much like them. Fat cat owners tend to have fat cats; thin cat owners tend to have thin cats. People who are nervous tend to have nervous dogs incidentally, though quite how that works, I don't know, but it certainly doesn't work in terms of genes. I assume as a biologist that this cat did not inherit any DNA from its owners but it certainly inherited a diet um er they fed it far too much as they were feeding themselves.

So you might say, Ok so being obese is simply a matter of diet but it ain't as simple as that. Here's, er you can certainly change it by diet and here a guy who has changed it by slimming erm so you can change it by diet but there are certainly plenty of cases where being obese has got nothing to do with diet. Here's a mouse not a cat and er this is a mouse that's got a gene mutation and a gene mutation is an error an inherited error in the DNA. This mutation was discovered about fifteen years ago now and the mutation is called the obese mutation. And it actually affects a particular protein er the gene makes a protein in the blood and we know that the blood is full of hormones; the first hormone ever to be discovered was where? Here at UCL in the Physiology Department just up the road 1903 and the first hormone ever to be discovered was a thing called Secretin which your Pancreas produces er when you have eaten a meal. And Secretin comes out and says alright stop eating now you've eaten enough and your appetite then disappears. Well we know that Secretin is only one of many, many hormones. This, this particular protein hormone is called Leptin and this mouse has got an absence of this Leptin hormone and as a result it just eats and eats and eats. It can, it does not know when it's eaten enough and it continues to eat until it grows fat. So you could say for the mouse maybe, well it's in the genes, but again if we didn't give it any food it wouldn't become obese. There are children, very rare, who are born with this condition and if you give them an absolutely rigidly controlled diet, and it's very difficult because they are hungry all the time, er then they don't become overweight or in fact most of them don't even do.

So nature genes and environment are both involved and in fact, the most important message of this talk is that genes and environment are always involved in everything and they interact, genes and environment always work together. A classic example of that, and I'll stop talking about cats in a minute, I'm not obsessed by them. The classic example of that comes from this cat here which is called a Siamese, erm it carries a gene mutation which is known as the Himalayan mutation, I don't know why its not called the Siamese really, but I imagine that many of you who have seen either real examples of this cat or pictures of them, they're very, they're quite popular amongst cat fanciers and there very, very beautiful. They've got black ears, a black nose a black tail, and black feet and if it's a gentleman cat like this one is, it's got black testicles as well. But the main part of the body mass, the main body mass is white ok. We know a lot about, a lot about the um, the um, the Siamese cat. We know that it's actually got an inherited error in the biochemical pathway, the machinery that makes skin pigment. Now we've all got skin pigment based on melanin. Melanin is a dark coloured substance. Erm its made in the skin and we've all got it, wherever our ancestors came from, we've all got various amounts of melanin, some of us have got more of it , some less, we've all got it in the skin. This cat has got an error in the pathway which makes melanin which gives it, its appearance. One of the enzymes that does the job has been damaged. However, it's been damaged in a slightly odd way. Most mutations, most many of them when they cause damage to an enzyme, they stop it working altogether and there are plenty of white cats out there who have got damage which means they can't make any of these black pigments at all. But this particular mutation only causes a small amount of damage; it just harms the protein, the enzyme that makes the pigment. It harms it so that it can only work at low temperatures. It's a matter of chemistry really. If the temperature is low then the molecule is more stable and it doesn't fall to pieces, so the cold parts of the cats body which are its ears, its nose its tail, its feet and needless so say it's testicles , the coldest part of the body as is well know, urm. The cold parts of the cat's body become dark and the warm parts of the cats body which are the main body mass stay light ok. Now many cat breeders, many people who like theses cats, they try to breed from relatively light coloured Siamese or relatively dark ones to try and breed a line of Siamese with only a tiny bit of black on their noses or ears or a different line the Siamese with a lot. But, and you can do that, you can do that, you could do some cat breeding if you want to, but of course you could do exactly the same by changing the environment. If you keep a Siamese in a warm room it actually comes out to be light in colour alright because if it's in a warm room, a horribly hot room like this one then the enzyme, the cat's body is warm the enzyme can't work the very coldest parts of the cat's body. If you keep a Siamese cat in a cold room or a refrigerator, you end up with a black cat, in side every Siamese is a black cat struggling to get out OK. It's an expensive way to get a black cat but it does work alright you get a black cat and um. and one rather clever Siamese owner took his kitten who name I happen to know was named Edward and shaved the letter E on its side and kept that cold while it was growing up and you can see its got its name it's letters E for Edward, is on its side in perfectly natural black fur its nothing to do with being dyed or anything like that, Its natural black fur. So old Edward can stalk around the streets of Bloomsbury getting a lot of street credibility from the other cats. So it's meaningless then, to say therefore that being a Siamese is genetic or environmental. It's not, it's both. You need to have the damaged gene and you need to be in the right temperature to show the Siamese pattern. People often think that separating nature from nurture gene from environment is a bit like slicing a cake. There's a slice that's called nature DNA that's and a slice that's called nurture; the environment the temperature or the way you live. Well that isn't true of a Siamese cat and that isn't true of people either. Let's go back to our obesity problem, here our picture of some

individuals from a Native American group called the Pima Indians. Pima Indians are invisitive of the country. Pima Indians are a Native American tribe who live Arizona over into Mexico. Here's a picture of two Pima Indians taken in 1900 and um you can see, I think you can see that they are young, healthy, good looking people obviously not overweight OK Now here's a picture of what might be their grand children or their Great Great Grandchildren taken in the year 2000 and these two individuals are severely ill. There grossly obese there very very overweight and because there both so obsess they both have adult onset diabetes unable to control the amount of Glucose in their blood and that leads top all kinds of very unpleasant side effects. It can lead to Ulcers which means you could lose your limbs, it could lead to blindness, it could lead to deafness and it can lead very quickly to death. So adult onset diabetes is dangerous and these people are tremendously susceptible to it before the Siamese cat reason. Because they have a set of genes er which means that if they eat too much and only if they eat too much of the western horrible cheese-burger diet. Then they will have severe problems with their weight. Europeans who eat that horrible cheese- burger diet, they might put some weight and some will put a lot of weight on, but they don't suffer nearly as much as the Pima Indians. Pima Indians who don't eat the western diet and eat the diet that they have had throughout history which didn't have much meat in it which was based on grain, corn and that kind of stuff, they are perfectly healthy. Now this gene, is common in different parts of the whole, it's common in Native Americans it's actually common in Asia because of course Native Americans are of Asian origin. They came across the Barring Land Bridge only about 15 000 years ago. There's another patch of it in West Africa um er and in all these places, it seems to be associated with a climate in which the weather is very unpredictable. The Pima Indians live in a desert and what happens is that for two or three years you might have good rains and plenty of stuff to eat and then for a year there may be no rain and so er what this has evolved to do is to store large quantities of ft when there is plenty of food around and when there's no food you can use that fat until the next rainy season comes along. But of course when there's food around all the time then it's a big big problem. So here we see a beautiful example of the way in which nature and nurture actually interact. For many people of course food is a drug alright it's a chemical.

Now let me continue this discussion by talking about some of the chemistry of nature and nurture, which is really central to our understanding of genetics. Now I'm not obsessed with either cats or the Royal Family but there's King George the Third and King George the Third's was our present queen's, I'll probably get this a lot wrong, one, two three, four, five.. Great Great Great, Great Great Grandfather Okay and he lived in the late Eighteenth Century and he was a very unsuccessful Monarch er because he hired Britain's second worst Prime Minister, who was called Lord North and er Lord North lost the American Colonies. So all the disasters of the world today are due to of a mutation with George the Thirds DNA because George the Third carried a particular gene mutation which illustrates very beautifully this interaction of gene and environment. You may be surprised to learn that George the Third is somewhat related to this chap here, who I a Werewolf.

Now what is a Werewolf? The Werewolf legend is quite common across the world in very different cultures and it turns on the idea that there are some people who are half human and half wolf. Now we think they are wolves because they live in caves, they only come out at night er they howl they drink blood um er there generally very fierce and to be avoided. Well why do we think that George the Third was associated with it this fact? George the Third it's pretty clear had a genetic illness called Porphyria. And Porphyria is an inability of the body to break down a part of the red pigment of your blood, you know your blood is red of course, most of that is protein and like many proteins it's got a kind of a central core which has got a metal in it, in the case of blood it's got iron in it Okay and this is some boring chemical formula of the central core of blood. This other known stuff, Haem its called is broken down in all of us in this room I would imagine into stuff that's called Hemin. It's excreted into your gut and then makes its way into the outside world in the usual way and doesn't cause any problems. A few people though, can't do that they've inherited a gene which doesn't break it down into this stuff called Hemin but something different that's called Porphin. P O R P H I N and that's nasty stuff, that doesn't go to the external world as it's supposed to, instead it gets laid down in various parts of the body and causes damage. One of the nastiest things about it is that hemin is sensitive to light. So that if you've got this damaged gene, your very sensitive to light. For example if you've got the genes and you go it bright sunlight, you will have enormous blisters and so on, on your hands. You may even lose some limbs. On your face things will be even worse and you'd go to great lengths to avoid going in the sunlight. You don't go out in sunlight, of course. In the old days perhaps you only went out in moonlight which is of course what wolves do. It's also the case that some patients, although I haven't managed to find a picture of it, Um some patients grow a thick layer of hair on their hands and on their faces as a defence against this sunlight Okay. Um another part of the Werewolf legend. The other part of the Werewolf legend is that they drink blood. Well, why would you think that somebody is drinking blood? Obviously if there producing red urine in the old day's people would assume that they must be drinking blood. But George the Third, when he was ill, he had the best available doctors and one of his, one of the schools of medicine in London in those days was know as The Piss Prophet's, a rude English word, 'Piss Prophet' and they looked at the urine of there patients, and of course doctors still do that, er doctors look at patients urine and indeed doctors until about thirty years ago, a doctor would regularly taste his patients urine, to see whether it tasted sweet, in which case they might have diabetes. Now they've got machines that do it for them fortunately. But George the Thirds Piss Prophet noted that His Majesty has produced red, bright red, port wine coloured urine, and here's a picture of some urine from a Porfiria Patient actually lit up in ultra violet. But this red colour we now know is due to this haem substance being excreted in the urine and its bright red, so that's another part of the legend okay. So lets, and the final part, the Madness is laid down in the brain and people often with this illness go completely insane and howl and shout all the time, another part of the Werewolf story, So why am I going on about this?

Well first of all, it does tell us about nature and nurture to some degree because you only suffer these symptoms er if you go into sunlight. So, although there are, so one of the treatments now and it can be controlled quite well, the illness, but one of

the treatments now is to keep the patients completely out of daylight. If they go out, it's in a mask with glasses and wearing gloves and so on and that helps. So that's the environment of change but there's a fascinating spin on this story because I said this is a rare illness and it is very rare in the western world, in most of the world except in one place and that is South Africa. And in South Africa among the Africaanas, er the Africaanas are the white South Africans of Dutch descent, who went out there in the Seventeenth Century. There are something like fifty thousand carriers of one form of this gene. Probably more than in the rest of the world put together and the reason they are there is just purely accidental. Every one of those fifty thousand people descends from the same woman, who came to South Africa in 1636, her name was Girit Banjanche and she must have carried a copy of this damaged gene. Now nobody knew anything about this until the 1950s because this is a very mild version of the Porphyria gene. But in the 1950s people started to use particular drugs, medical drugs, one in particular for very psychiatric illnesses, a group called barbiturates. Barbiturate drugs in the 1950s and 60s were quite widely used in sort of mood control and they were quite effective. There dangerous because if you take even a small overdose they will kill you, so they're not really used very much anymore. But they were quite widely used for twenty years and unless somebody took an overdose, they were pretty safe. Except in South Africa, where large numbers of people who took the Barbiturate drugs erm large numbers of people that took the barbiturate drugs died. Why was this? It turned out that the biochemical machinery which breaks down the barbiturate drug is the same as the machinery as that which breaks down the red pigment of the blood and is damaged in porphyria and these people who knew nothing about it carried a porphyriac gene that didn't show its affects until the new drug was produced, the new chemical was produced and then they paid the price. The treatment obviously was to withdraw the drug, which they did immediately okay. So again, nature and nurture.

Well let's talk a little bit more about drugs, let's talk about the most dangerous drug of all. I don know whether, I assume as you all appear to be extremely intelligent people erm I'm sure that not one of you smokes and I'm delighted to learn that erm good. Er alright, I have to say that I am a virgin, I don't know why but I've never smoked in my life, I've know idea why but I never have. Erm of course life wasn't like that, there was a time when smoking was even said to be good for you. More doctors smoked 'Camels' than any other cigarette Okay. God help us, smoking's a weird business, I've never understood it erm I don't know whether you've heard of the game played in Russia called Russian Roulette, what you do is get a pistol with six chambers, a revolver, and you put one bullet in it and you spin it round and you shoot it at your head and if it doesn't go off that's good and you pass it to your friend who shoots it and blows his brains out excellent game, strongly recommend it. If you smoke, if you smoke your playing Russian Roulette but your putting three bullets in the chamber not six er not one, simply because smoking kills one in two smokers. That is a lot, I'm not tempted to start, I can tell you. Well I guess you all know that smoking causes lung cancer and it certainly does. Lung cancer is actually quite a good way to go because if you are diagnosed with lung cancer you only have a one in two chance of lasting for five years erm and most people will be dead within five or six years. So that's quite quick, most smokers actually don't die of lung cancer, they die of something else, that's an illness that's called emphysema. And emphysema, here's a emphysema spar. Emphysema basically consists of drowning in your own spit erm I don't know whether you've ever heard anybody with a smoker's cough. They have got emphysema. What tobacco does is it actually poison's and destroys the system in your lung that clears the liquid that is always being produced there to help you to breath. And in time it actually breaks down the lung tissue and you get, instead of a nice beautiful spongy lung which is pink you get these horrible great blisters of tissue instead. And you basically can't breathe, you basically drown except maybe it takes you maybe fifteen or twenty years to drown the last five years of which you'll be on an oxygen mask and you'll be unable to move because you wont be able to get enough oxygen and that's emphysema and it really isn't a good way to go. It turns out though that actually emphysema is again strongly genetic. What actually happens is, some people, there's an enzyme which is called this, never mind its name, or how to pronounce it, which is part of the lung system of clearing itself of making itself work. Now in our laboratory at UCL we've being looking at genetic variation in this enzyme and there are two types, call them type A and type Z which is the norm and about one person in six has got one copy which is the type Z, No one copy in eight Z gene er about one person in seventy has got two copies of the type Z gene. Well if you've got two copies of the type z gene and you smoke, you are going to die; I can guarantee you, of emphysema before you're forty, alright. There's a rather depressing, these are erm um er if you've got two copies of ZZ your at some risk of emphysema anyway, you might get it by the time you're sixty. This is, we will just look at this line here, this is the emphysema incidence of the people with two copies of the damaged gene, and even if they don't smoke, there at some risk as they get older. If they do smoke though, you'll see that by the age of forty five, half have emphysema and they die off pretty quickly thereafter. What we've actually done is to start a programme, that's called The London Genetics Knowledge Path and what we do, what the London Genetics Knowledge path does is to go out to schools, as you do, and test school children and find out what there constitution is for this particular enzyme and if they have got two copies of the Z Z , two copies of the Z type of the enzyme, we say to them look Fred or Mohammed or whatever your name is, this is your situation, if you smoke, we will guarantee you, there will be no question about it that you will have emphysema and you will be severely crippled by the time you're forty or fifty, what are you going to do about it ? And the response has been and I'm sorry to say has been nothing, they don't care. It doesn't make any difference at all and they continue to smoke. It's a bit depressing the only effect we've managed to pick up is that, we don't tell their parent's the information is theirs, it's not our job to tell their parents. Obviously they themselves sometimes tell their parents and the only effect we've managed to pick up has been that their parents smoke more because they're worried about what's happened. So it hasn't been a complete success. Let me end up by talking about another and different chemical addition which some of us, males, so of us have got .This one here, it's a chemical which is called testosterone. And about half, about half or less the people in this room have got a lot of it and about half of the people in this room have a little of it. The ones who have got a lot we call technically men and the technical name for the other ones are women alright. And testosterone is what makes males, males and it's remarkably simple, it's a very simple chemical it's a steroid hormone. I

guess we know were it's made, it's made in the Teste's um what's, what's interesting is how simple the machinery of being male actually is, the male or human male have got a Y chromosome, which is small and short and completely useless apart from one thing and that one thing that it's got on it is a gene, which is, if the embryo has got this gene, it's called SRY um the gene is switched on in the human embryo about six weeks after fertilization often when the mother doesn't even know she's pregnant or beginning to suspect she's pregnant. The gene is switched on, about six weeks after fertilization for only about a week and in that period it switches the developing embryo from being female which is the default state to being male and then it switches itself off and the testes then takes over and produces lots and lots of testosterone, Well testosterone is interesting stuff okay here's, I occasionally look myself up on the web, and if you look up Steve Jones on the Web um it's a very common name Steve Jones, one of the commonest names in England in the English Language. Here's Steve Jones, here's a guy you get, a guy that's completely, well I'm completely filled with testosterone, but I imagine he's more filled with testosterone than I am. Alright, and he's quintessentially Male, He's big and he's brute and he's stupid um he's obviously looking, he's obviously looking for a mate. What kind of mate I'm not quite sure, as he's a bodybuilding champion it's pretty likely that he's actually abusing testosterone, he may not be I don't want to slander him but most bodybuilders and weight lifters abuse testosterone and they pay a price for it, um it's certainly very bad for there health and they have a much higher death rate than normal. But even those of us who don't abuse it, suffer from having it. Here's a cheery, we started off talking about death so let's end up by talking about death here's a cheery little slide which shows the patterns of life and death of people with this gene testosterone and people without , men and women. Here's the mortality rate per hundred thousand people from ages at birth zero to the age of eighty and as we all know of course men die at a greater rate than women do. And there a difference in life expectancy of about five years in western, in the west, between men and women which has been getting bigger but last year stopped getting bigger, this year it's actually gone down slightly and that mark's the death of those women who started to smoke in the 1940s and 1950s before that very few women smoked okay. And we die from various genetic, various interesting gene related causes. For example men die from accidents much more than women do. So if you've got this testosterone gene you'll die accidentally, four year old boys die at twice the rate of four year old girls from accidents. It's even the case, and I know this to be true, that men are struck by lightening at three times the rate that women are. And it might seem odd to say that there's a gene for being struck by lightening but when are you struck by lightening, your struck by lightening when your doing all them male things like climbing up a mountain, standing on the top to show off or your standing on a golf course demonstrating your virility with a big piece of metal in your hand. And if lightening strike um. So men die from accidents, Men die, interesting enough much more from parasites and infectious diseases. Now that's quite new, we didn't know that until recently or nobody put it all together and um it turns out that this hormone made by this single gene, um is a very efficient way of switching off your immune system. And your immune system as we know is the bodily defence mechanism, that makes anti-bodies that fights off bacteria, tape worms, tooth derunda, various enemies that try to get in. The male immune system is much less efficient than the female immune system; men are much less good at fighting off parasites and diseases. One of the effects of abusing testosterone and this is one of the ways you can tell that someone is abusing testosterone. If a bodybuilder or a weightlifter is abusing testosterone, very often they get acne, acne of course is a spotty face which a lot of teenage boys suffer from and that's because by taking this drug, this natural chemical they're actually turning off their immune system and so the bacteria that cause your face to get spotty can get in there, and they cause the acne and if you look at weight lifters you see they've got very spotty faces and that's because of the effect in the, in the, in the switching off the immune system. But the interesting, one interesting difference which is very much coded for by DNA, is the gene for murder alright. Now clearly there's a gene for murder, it's absolutely straightforward because nearly all murders are done by men and nearly all those people who are murdered are men and you can see that here. Here's the death rate of men versus women through murder um from the ages from nought to eighty and you can see there's a huge peak in the murder rate by young of being murdered by men of around the age of twenty or thirty and they're murdered by other men of that age. You could argue they're trying to show what excellent husbands they would make by going out and killing the opposition now that would be the evolutionary argument but I'm not convinced it's a very telling one. So you can say there's a gene for crime it's a carried on the Y chromosome, nearly all crime, effectively all violent crime is carried out by men, men have got, all men have got this gene and therefore it's the gene that causes crime, and it's really a pretty consistent thing but actually I'll end up by showing, suggesting to you that this is actually a perfect example of the way that nature and nurture interact. I have no problem with stating that men are born more violent than women, the evidence is absolutely crystal clear that's true and it shows itself in different ways. Here's the murder rate um er by by men and women of different age in in England and Wales Okay and you can see that men are much more dangerous than women at all ages okay theses are the men these are the women, women, have rather, generally don't do much murdering. Young men are the most dangerous, there are a number of bad tempered eighty year olds around who go out and er kill people off but the evidence the picture is very very clear and it's clear internationally. If you go to Detroit in Michigan a big American city we can see exactly the same thing. Young men tremendous murderers, the old people in Detroit are even more worse tempered that people in England. So you would say okay here's a beautiful example of the way in which a gene causes crime all over the world except one thing you may have noticed let's look at theses figures the murder rate per million people per year because if we go back to the English figures the murder rate per million per year is nought, five, ten, fifteen, twenty, twenty five, thirty. The murder rate in Britain is very low, it's lower still in places like Japan where it's very very low indeed um in Britain Okay so the murder rate is very low in Britain. But although the pattern is there, If we then go back to our American data, those figures don't go nought by ten they go nought two hundred, four hundred six hundred eight hundred a thousand twelve hundred. Now these are somewhat old figures the situation has improved in America okay. So what's actually happening here is a statement of a way that nature and nurture interact. The reason you have a huge murder rate in a city like Detroit is very simple. Weapons are very easy to get, you can buy a gun across the counter in Detroit and people use them in positions of great social inequality it becomes very very violent. The people who use them are the men but the answer to the murder rate in Detroit is not to kill all the men or

castrate all the men. The answer is to ban the sale of weapons and as you know it is effectively impossible to buy firearms in England buying pistols you cannot do under any circumstances and that's one reason why our murder rates so low. If you look back a British history to around sixteen hundred where I started talking about three quarters of babies been dead before the age of twenty one quite a lot of those people who died were murdered. In sixteen hundred the British Government erm passed a law and the law banned short swords. In those days everyone carried a sword okay and until about sixteen hundred it was fashionable to have a sword that was about that long. Then they were, the Government saw that they would not get away with saying you can't carry swords that would not be acceptable, like banning smoking they wouldn't dare do it erm you can't carry a sword but they did say you can only carry a sword if it's that long, three feet long and of course it takes that much longer to pull out a three foot long sword by which time you thought oh maybe a wont murder him after all. Or alternatively, the guy has seen this and he's thought bloody hell and his off. So that simple little social change dropped the murder rate by half erm so I think these two graphs then summarise the question about genes and the environment about nature and nurture. Where are we? That one versus that one er and the best summary I can take I suppose ids that when it comes to genetics er um science can tell you everything you need to know about yourself apart from the really interesting stuff. So I'll stop there thank you.

Do you traditionally ask for questions yeah? Are there any questions Is it going to be in the exam?
Erm if a person is gay does it relate to the DNA.

The question is, it's about the gay gene, Now if a person is gay, is homosexual is that related to the DNA the genetic code. Well it's a very interesting question erm it's very hard to say I was friendly only quite friendly with a guy discovered the gay gene who as it happens was himself gay and he's a very good geneticist. He found he thought how did it work again?, that the sisters of gay men were rather more masculine than usual he thought and he thought that he found what's called a sex link gene carried on the X chromosome which tended to predispose one to being a male homosexual. Now I, erm this happened about fifteen twenty years ago erm and another chap I know a gay activist in the states called Doug Fortuma. He was terrified of this because he thought this would be used to stigmatise gay men and say your born defective and all this kind of stuff but the interesting fact was when the gay gene thing came out, the gay community welcomed it because, generally, because they said look it's not catching. I was born this way I'm not going to go out and persuade anybody to be gay it's in my DNA. The sad thing or the fact of the matter with the gay gene is that it has not stood up in other words people have gone back and looked at that gene in other families and simply haven't found them. So if there is a genetic effect then it's a very weak one. There's a, actually the gay the homosexually story as a statement of the importance of the environment. In the British Navy which as you know ruled the world for quite along time. In the British Navy Homosexuality was a hanging offence, in other words if you were caught in bed with another sailor erm at sea then you would be executed right and that was a terrible thing to happen. It was a terrible thing, it was a hanging offence until the ship had been out at sea for forty seven days and on day forty eight it became completely legal. In other words you can do without sex for forty seven days, male or female but on day forty eight alright alright we don't want, we all know what you get up to, so it becomes legal so in other words in places like ships at sea or prisons or in armies, men will become homosexual who otherwise would not be homosexual, so it environmental might well be, might possibly be genetic as well. Any less contentious questions ?

If I may ask you about what do you think about...?

Yeah the question is about what I would call false parenthood or false fatherhood in society? How many children out there are not their father's child? Okay and you could of course do that with genetic fingerprinting, I'm sure you've all heard of this DNA fingerprint discovered by Alex Jefferies at Leicester some twenty years ago now. All you need to do is to compare the child with his father and you could be absolutely certain er 99.999 percent certain whether the actual father is the biological father. Well I once wrote a book that's called The Descent of Men, it's about maleness and manhood I actually went to great lengths to try and find out what the true figure is for that, and it's very very hard to find out, one of the places that people get there figures from, there are various companies which will test your DNA, there was one here at UCL which we closed down because we didn't want to get involved in that rather dirty business er in the States you can dial, on American phones they've got letters as well as numbers, one of them is 1800 Are you my dad? If you dial 1800 Are you my dad and send them a spit sample and they'll tell you whether your supposed father is your real father or not. And its very hard to track it down if you go to 1800 Are you my dad and ask them "how many of your samples are false fatherhoods?" in other words the biological father is not the real father the answer's a lot. Its about one in three okay but of course that no good at all because the people who set this stuff off, there already suspecting the something strange going on you know there's two men a breakfast not one kind of stuff. So that's not a decent sample. the other place I could find the information was from Switzerland. There's a genetic testing clinic in Switzerland which published a paper erm saying, comparing parents and offspring to look for false paternity and they've found on a rate of one in a thousand but on the other hand that's Switzerland what do you expect from Switzerland, it seems to me low. Now there's this figure of one in twenty five but I think you have to stand back and ask, In Britain, what do you mean by family, you know there are different family structures going on. In the West Indian community and indeed increasingly in the European community there is often serial monogamy there would be one father who would go away and then another father would join in. Um so I still don't think we know the figures one in twenty five strikes me as about right but I only say that because it sounds right, I don't really, I don't really know how dependable that is. Are you shocked by one in twenty five? What is it in the Far East do you know? Nobody knows I guess they wouldn't dare find out, it will be the same; people are the same everywhere take it from me. Any less shocking questions?

Er in the case of when someone's a serial killer is that chromosome difference or genetic difference?

In the case of a serial killer, God another shocking question um well a serial killer, all serial killer, er I don't think there sever been a female serial killer as far as I know perhaps maybe there's been one but there's been hundred's of men. So they've all got one Y chromosome, there was once a claim that, there are some men that are born with to Y chromosome's Kind of supermen okay and I had a colleague who studied in a mental home in Scotland called Carstairs which is the Scottish equivalent of the English hospital that's called Broadmoor and Broadmoor as some of you may not know is the hospital for the criminally insane where people who have done terrible, unspeakable things end up and don't, basically, generally don't come out, unless they've been treated successfully, um and she found in the Scottish equivalent, er a great excess of men with two. What she called a great excess of men XYY Men with two Y chromosomes and so from that came the claim, that actually men with two Y chromosomes were dangerous. But in fact, that wasn't true at all, firstly the excess, there was one two many, over expectation in there, and secondly, If you look at men with two Y chromosomes, they tend to be too male. In other words they tend to be too tall, too big and too stupid, alright, and they tend to have jobs which are, they've have rather low intelligence which are and they tend to be in jobs like bricklaying, heavy industry and that kind of stuff. If you compare them with other tall heavy and stupid men, without an extra Y chromosome, the murder rate by the two is exactly the same. So I don't really think you can give it any, any, any er genetic basis.

Can I stop there, no one more?
I had to ask you said that Lord North was the second worse Prime minister?

Mrs Thatcher was the worst, there was a time when every body would nod and say yes Mrs Thatcher, but of course it's not as easy now.
Okay Thank you very much