POST-PRODUCTION TRANSCRIPT

M248/TV5 IN SEARCH OF CERTAINTY

Costing number: I/FOU M638J

Spool: 10374

Duration: 29' 01"

Producer.....Liz Gray

Narrator.....Glenda Jackson

Editor.....John Hackney

Music:
kpm
362 Tr3
2'22"

GLENDA JACKSON
Scientists are on the verge of understanding the human genome, the complete genetic map for a human being. During the last century one human being in particular helped pave the way.

STEPHEN SENN
Fisher is the greatest of them all, he's the number 1, you can't really think of anybody who's more important in the history of statistics.

ALAN GEFEN
There's a general rule in biology that if you have a bright idea then there's nine tenths of a chance that it's in Darwin, but if it isn't, then there's a nine tenths chance that it's in Fisher.

MICHAEL HEALEY
The whole of modern research in agriculture, in medicine, and to a large extent in industry as well is based on the principles which Fisher laid down.

GLENDA JACKSON
Even someone as far-sighted as Ronald Aylmer Fisher might have been surprised by his legacy. Yet today few people beyond the scientific community have heard of him. Joan Box has devoted much of her life to the quest to uncover more about Fisher

JOAN BOX
RA Fisher, yes, he was my father. I was the closest of the family to him and I felt I wanted to collect anything that was known of him and keep it, to preserve it.

GLENDA JACKSON
Now living in the United States, Joan has returned to Britain on a journey into the past.

JOAN BOX
Still: Fisher c. J Box
I should imagine the first impression people would have would be of an untidy person, scruffy looking, untidy beard. Strong glasses, really he couldn't see very well at all and in his late years was practically blind. But he had more important things to do than worry about his appearance.

Still: Fisher and Joan c. J Box

GLENDA JACKSON
On the outskirts of Harpenden is the world's longest running centre for agricultural research. It was here at Rothamsted that, as a statistician, Fisher was at his most creative.

BOB:
We only have a small herd of cattle now.

JOAN BOX
Oh is that right. So you keep them just for farmyard..

BOB:
Just for the farmyard manure. You'll remember the manor house of course.

GLENDA JACKSON
Still: J Lawes c.Rothamsted
150 years ago its founder, Sir John Lawes, believed he could make his fortune by investing in a new discovery, artifical fertilizers. He needed the money for the upkeep of the Manor House, the Lawes ancestral home dating from the 17th century. Anxious to secure his investment, he began a series of fertilizer experiments. Lawes divided some of his fields into strips, each one using a different treatment.

Rothamsted became particularly important when the first World War increased the need to improve British food production. Fisher became Chief Statistician here in 1919.

Music
kpm 362
Tr45 19"

Still: harvest
c
Rothamsted

BOB
So here we are Joan at Broadwalk. Well, it's been in winter wheat since 1843.

GLENDA JACKSON
Wheat has been grown on Broadbalk Field for over 150 years, using a variety of fertilizers.

BOB:
We'll go and have a look at the section that has never had any weedkiller. We put 2 or 3 herbicides on this area during the year.

GLENDA JACKSON
The results have been monitored continuously and Fisher's first challenge was to re-examine the mass of accumulated data, "raking over the muck-heap" as he later described it.

BOB:
35 tons of farmyard manure every year goes on here.

JOAN BOX
That's splendid.

GLENDA JACKSON
But in terms of the numbers required for reliable statistics, even this mass of data didn't amount to much. Fisher was nevertheless

able to devise groundbreaking ways of working with it.

MICHAEL HEALEY

Fisher's time at Rothamsted was fundamental to the growth of statistics as we know it today. Statistics grew up in this country if you like, in the early 1900's under Karl Pearson. Pearson like to deal with large numbers, and this simply doesn't happen. You have an experiment on the farm at Rothamsted which might have 32 field plots and you've got to make the most of them. And this is what Fisher did in his pioneering work in the 20's, he developed the methodology which we all use today for extracting the information from a limited amount of material. And to do this, he had to re-invent the discipline of statistics.

Still: Pearson c. Science Photo Lib

Music kpm 63 Tr16 36"

GLENDA JACKSON

He did this by emphasising the importance of involving the statistician right at the start of an experiment and devised methods for designing experiments which are still widely used today.

STEPHEN SENN

Fisher once said, if you called a statistician in at the end of an experiment he could perform a post-mortem. He could tell you what the experiment died of. And what he really showed was that you had to call statisticians in at the beginning if you wanted to get the most out of your data.

GLENDA JACKSON

The Winter Wheat experiment will discover the fertility of different types of wheat treated with different amounts of fertilizer, but it must also take into account additional factors such as the levels of fertility in different parts of the field. Fisher pioneered ways of working across a range of factors and exploring how they influence each other.

Music kpm 63 Tr16 32"

STEPHEN SENN
Often Nature won't reveal her secrets if we vary factors one at a time, we often have to vary them together, but in a plan which has been carefully chosen.

GLENDA JACKSON
The modern design of Winter Wheat, based on Fisher's ideas, incorporates numerous blocks, accounting for different combinations of background factors.

MICHAEL HEALEY
Fisher was always the sort of personality who liked measurement, who liked certainty, but who appreciated the fact because he worked in a biological environment like Rothamsted, that there is no such thing as certainty in scientific research. And this I think was what drove Fisher psychologically if you like, the quest for certainty in the presence of uncertainty.

STEPHEN SENN
Fisher like all scientists was driven by a quest for certainty. He was faced with variable experiments all his life and he showed that that didn't provide the scientist with a reason for despair, he could in fact marshal the data, he could deal with variability in such a way that nevertheless, at the end, reasonably certain conclusions would be reached

GLENDA JACKSON
He was determined to understand the unpredictability of Nature, to measure the un-measurable.

STEPHEN SENN

It was well known that the fertility of plots could vary from plot to plot and so methods had to be found of taking account of this. What Fisher showed was that you also had to carry this through to the analysis.

GLENDA JACKSON

Nowadays researchers analyse the data with computers, using methods Fisher himself invented at Rothamsted. An instant "analysis of variance" can be produced displaying the interaction between the varieties of wheat and fertilizer in a style very similar to Fisher's own.

MICHAEL HEALEY

Music
scd 130
Tr22 50"

I remember very well my excitement as a student when I first saw one of these electrical machines doing division all by itself. You press the button, it whirred backwards and forwards, and out came the answer. The Millionaire computer was Fisher's own purchase when he was appointed here in 1919. He shocked the Director by saying, what I must have is a calculating machine. Such a thing had never been heard of.

Still: Fisher and computer c. Fisher Memorial Trust

GLENDA JACKSON

At Rothamsted, the search for certainty enabled British farmers to maximize their productivity and Fisher's methods were swiftly adopted worldwide. Fisher thought of himself not as a statistician but as a scientist and in 1929 he was elected a Fellow of the Royal Society in recognition of his achievements at Rothamsted.

Still: Fisher c. J Box

STEPHEN SENN

He was someone who was fascinated by biology from a very early stage of his life. But he also was a very good mathematician and somehow he realised that he could apply his mathematical insight to biological problems. And this was something which really opened a whole new world for him.

GLENDA JACKSON

Rothamsted could more easily accommodate Fisher's new world than a university might have done. It also gave him time and space to develop his own research into genetics. But he brought his obsession home with him.

Still: Fisher and mice c. J Box

JOAN BOX

He started breeding mice at home. As the eye colours and coat colours grew more and more numerous, and the mice grew more and more numerous.

Still: Fisher and mice c. J Box

GLENDA JACKSON

After 14 years at Rothamsted Fisher finally began an academic career in genetics and the mice went with him. From a professorship at University College London he went on to teach at Cambridge.

Music scd 130 Tr5 48"

JOAN BOX

Yes, he led a double life, from the beginning. It was both genetics and statistics. There was never any cessation.

GLENDA JACKSON

Anthony Edwards is a Fellow of Caius, Fisher's college, and was his last undergraduate student.

ANTHONY EDWARDS

I'd heard this name but I could see no reason why this famous statistician should be teaching genetics, and in any case I though he must have been the contemporary of Isaac Newton. It hadn't occurred to me that this man might still be alive. I just turned up, on spec as it were in the afternoon, and when I went through the open door of the Department of Genetics, to ask for the person whom I'd been told to go and see, I thought he was the hall porter.

Still: Fisher MCU c. J Box

GLENDA JACKSON
His appearance held clues to the roots of his genius.

ANTHONY EDWARDS
He was a short man, a wiry, tough man, bearded, pipe smoker. He had very short sight and had always had very short sight. And one of the things I keep in my room in college was his last pair of spectacles. And I thought you might like to see how very, very small and how the glass is very thick at the edges, appropriate for somebody who is, was extremely short-sighted.

Still: Fisher as boy c. J Box

GLENDA JACKSON
His capacity to imagine, to visualize multiple dimensions of geometry gave him a unique perspective.

Music
kpm 63
Tr16 46"

ANTHONY EDWARDS
He had to depend very much on learning by ear. And he did develop a most extraordinary ability to do complex mathematics and complex geometrical arguments in his head without writing things down.

GLENDA JACKSON
It enabled him to make intuitive, new connections across areas of science which had been considered distinct. As a biologist and statistician, Alan Grafen shares Fisher's range of interests.

ALAN GRAFEN
Fisher thought in pictures and he solved very complicated problems using pictures in his mind. It's possible to imagine that because he couldn't see very well out there in the world, he turned his eyes inward and saw very clearly in his mind. The formulae came out of some deep recesses of his subconscious.

GLENDA JACKSON

Still: Fisher as young man c J Box

Fisher went up to Cambridge in 1909. His extraordinary insight inspired even his earliest achievements.

ANTHONY EDWARDS

Music kpm 63 Tr10 1' 05

When Fisher came up to Caius as a scholar he would have been allocated a room, and as a scholar it would have been in one of the, one of the inner courts. And as it happens, the room in question is next door to the staircase that I'm on now. With that splendid naivety which your 20 year old will have, he will just set off on a course solving problems in a way which will have been entirely original to him and although the method of maximum likelihood can be found in earlier works it is a development which started on that staircase in 1912, which led to his great 1922 paper on the mathematical foundations of theoretical statistics, from which the modern theory of estimation flows.

GLENDA JACKSON

The concept of maximum likelihood is one of his best known developments and is still at the cutting edge of the scientist's search for certainty.

ANTHONY EDWARDS

Any method of estimation in statistics such as the method of maximum likelihood, is a method to teach us how to extract information from data, to find out what we don't know from what we do know in the form of data.

GLENDA JACKSON

At the British headquarters of the Human Genome Project, the Sanger Centre in Cambridge, Richard Durbin leads the team of statisticians.

RICHARD DURBIN

Ideally in science we want to establish the truth conclusively, often we only have partial sorts of information and one of the challenges is how to put together partial information that may not be completely conclusive in itself, to give as much certainty as possible. The Human Genome contains the information that is inherited, that creates a human being from a fertilised egg. And we can of that as a parts list, and an instruction manual putting together those parts to make a complete human.

GLENDA JACKSON

Music
S Faux
47"

Scientists now know the complete human genome sequence.-But the code needs to be translated into a useable form, this means analysing the individual genes which make up its component parts.

RICHARD DURBIN

When we look at the genomic sequence, it's a long string of A's,C's, G's and T's, just 3 billion letters long. Within that, we know there's around 50-100,000 genes and these are comprised of small segments of the sequence.

GLENDA JACKSON

Using statistics, Durbin's task is to investigate the nature of unknown genes – by applying data from genes which are already understood.

RICHARD DURBIN

What we want to do is use all the information and evidence that we have to help us find and characterise genes in other parts of the genome where we haven't yet done any experiments. The way we do that is by fitting parameters to a model using maximum likelihood or related techniques and really the theoretical foundations for this sort of approach were set earlier in the century by Fisher and his colleagues

GLENDA JACKSON

Music
kpm 63
Tr25 25"

Despite these pioneering achievements Fisher's work is not widely known beyond the scientific community. His perspective and insight are difficult to grasp or to explain simply, familiar obstacles for anyone who tries – the theory of maximum likelihood for instance.

ALAN GRAFEN

If you want to draw inferences in the presence of uncertainty the first leap you have to make is to create certainty in your imagination. But not to create one certainty, to create lots of different certainties, and that's not as easy as it sounds. You have to say well, if this were the case, everything would be certain, or if that were the case, everything would be certain, or if the other were the case, every thing would be certain, and drawing up that list of possible certainties is the first stage in drawing inferences in the presence of uncertainty.

The next stage is to take each possible certainty and to ask, what would happen if that were true, then the next, what would happen if that were true, then the next, what would happen if that were true. And then you look at what really happened, and you look back and say, well, if this were true how likely is it we'd see what we see now, if the middle thing was true, how likely is it we'd see what we see now, and if the last thing were true, how likely is it we'd see what we see now. And maximum likelihood is saying, well, which of those possible certainties makes it most likely we'd see what we saw.

GLENDA JACKSON

Fisher's effortless grasp of abstract ideas is reflected in his writing.

ANTHONY EDWARDS

Fisher's writing is extraordinarily tense and close, partly because he would formulate his ideas in his mind and very often dictate everything that he was to publish. His mentor, Leonard Darwin, who was Charles Darwin's fourth son, once wrote to him 'one idea per sentence is a good idea I think. You have to think hard whilst you're reading'.

Still: Fisher writing
c. Fisher Memorial Trust

ALAN GRAFEN

In this his most famous book, The Genetical Theory of Natural Selection, Fisher says in the preface, 'no efforts of mine could avail to make the book easy reading'. We understand it better now than when he wrote it and as biologists learn more, they'll understand the book better still.

GLENDA JACKSON

Music
kpm 63
Tr25 9"

Still: Fisher in study
c. Fisher Memorial Trust

If Fisher's giant steps of thought were ahead of his time, they were not always welcomed by his contemporaries.

JOAN BOX

New ideas are unexpected, they're difficult to assimilate, they're difficult to act on, and people get quite indignant and angry about them

ALAN GRAFEN

You can only tell people things one step away from what they know already and if you try to go 2 or 3 steps you lose them and they get cross.

ANTHONY EDWARDS

He thought so clearly himself, that he had great difficulty in appreciating the lack of clarity or as he once put it, 'the dense fog in the minds of the young men around me', and the rest of us suffered.

Music
kpm 63
Tr25 9"

GLENDA JACKSON

Still: Fisher in classroom c. Norman Draper

But it wasn't just his students who struggled, the intellectual giants of the day couldn't always keep up with him either.

MICHAEL HEALEY

Poor Pearson, who liked pages and pages of algebra, found that Fisher was coming along and proving his results, and saying 'it is obvious that' which is enough to make anybody cross.

ALAN GRAFEN

The trouble is he was usually right, but he wasn't always so good at explaining why he was right. And people misunderstood him, he didn't always take it in good part.

JOAN BOX

He did not tolerate fools gladly, and he could be quite rude. But that is human

GLENDA JACKSON

Music kpm 63 Tr25 12"

Still: Fisher looking at blackboard c. Norman Draper

The inner world of his intuition and intellect seemed at odds with the world outside. Despite his best efforts, he wasn't always good at explaining himself.

ANTHONY EDWARDS

He had this amazing analytical ability to complete long mathematical arguments in his mind without putting anything down on paper. And frequently he would produce an argument which was correct mathematically and then not be able immediately to reconstruct how he'd arrive at that point

STEPHEN SENN

Still: Fisher

by blackboard c. Norman Draper

Fisher had brilliant insight on many matters and he often chose to explain things in an intuitive way which used a minimal amount of mathematics. And he hoped in this way that his ideas would become comprehensible to a less specialist audience. But the net result often was that the mathematicians didn't understand him either

Music kpm 63 Tr25 10"

ANTHONY EDWARDS
Thinking about it in later years I had the sense that he was probably rather lonely.

GLENDA JACKSON
While Fisher's perspective on the world may have left him out of kilter with his time, the legacy of his ideas has been phenomenal. Perhaps even he couldn't have dreamt of its scope.

Music scd 130 Tr18 20"

ALAN GEFEN
The value of abstraction in solving problems as Fisher did, is that you begin locally with a particular problem you want to solve, but by thinking about it in a very abstract way is like ascending into the stratosphere, so that you can then solve all kinds of other problems all over the world with just the same solution as you've just achieved.

GLENDA JACKSON
Car manufacture is just one of the current applications for the ideas that Fisher developed at Rothamsted.

Music S Faux 23"

As technology advances, engineers are developing new engine designs which have to take into account an increasesing number of factors.

Cars on road/ production line c. Ford

DEAN ROSE
The first thing we're trying to do is produce engines which are

environmentally friendly. There's a drive at the moment for having green engines which are very efficient. The other side of the scales, we're really trying to balance that with customer requirements. They're very specific about having engines with low fuel consumption, are energy efficient and can produce as much power as possible. So it's really trying to get the balance between those major aspects of optimization.

GLENDA JACKSON

Music
S Faux
18"

Fisher's methods for designing experiments are at the heart of the complex work of the development team – using pioneering techniques made possible only by the latest computer software.

DEAN ROSE

There's no way we could do this work without computers, the number of factors which we're varying are absolutely astronomical and using traditional techniques it would take something like 90 years just to visit all of the operation points.

GLENDA JACKSON

It now takes only 2 weeks to perform the same kind of experiment. Practical tests are used merely to verify and adjust the computer-generated data, creating a virtual model of the engine's performance.

DEAN ROSE

Now this is really useful for us because we can then ask the model what the engine's doing, rather than do down to the cell and re-test point after point.

GLENDA JACKSON

Music
S Faux
33"

Computer technology means that Fisher's principles can be easily

combined with other concepts of statistics. New software packages can apply the theory of maximum likelihood at the click of a mouse.

DEAN ROSE

From my perspective it's really useful because coming from an engineering background I've had to pick up a lot of these statistics and the software enables someone with a fairly basic understanding of statistics to really get down to some quite state of the art techniques.

GLENDA JACKSON

Still: Fisher in profile
c. Fisher Memorial Trust

While Fisher's contribution to the theory of statistics may ebb and flow with the tide of ideas, there are reasons why his reputation has since been tarnished.

STEPHEN SENN

Fisher was not perfect. He had a spectacular mistake regarding smoking and that was, he decided to be clever rather than wise.

Smoking montage
c. BBC

When Bradford Hill and Richard Doll produced the first evidence linking lung cancer to smoking, Fisher countered that it could in fact be due to genetics.

Music
S Faux
23"

ALAN GEFEN

What he said was 'we shouldn't pretend there's certainty when there isn't and we shouldn't be causing mass scares of the population when actually there was room for doubt about whether or not smoking caused lung cancer. It was a very reasonable position, it's perhaps unfortunate he was funded by the tobacco companies at the time.

GLENDA JACKSON

Fisher's reputation has also suffered because of his strong

convictions about the practical applications of human genetics, known then as eugenics.

ARCHIVE V/O

Archive: Heredity in Man c. OOC

Eugenics seeks to apply the known laws of heredity so as to prevent the degeneration of the race and improve its inborn qualities. Not all mental deficiency is heredity, but heredity accounts for more of the mild people minded type. It would have been better by far, for them and the rest of the community, if they had never been born.

Music S Faux 34"

GLENDA JACKSON

Though shocking now, the principles of eugenics were widely accepted at the time.

ALAN GEFEN

Fisher had a great sense of social responsibility. One of his earliest papers is a rather pious one called "Some Hopes of a Eugenist". And he felt that we ought to use genetics in lots of ways including improving the human condition.

Still: Male family portrait c. J Box

Still: Female family portrait c. J Box

Still: Male family portrait as before c. J Box

JOAN BOX

He brought home all sorts of tests for the family, intelligence tests were being developed, he was very enthusiastic about the blood group work. Eye colours, hair colours, he brought Professors of Opthalmology to sort out our genetic traits as far as any genetic traits could be discriminated at the time.

STEPHEN SENN

Fisher wrote a number of articles in which he described what sort of political measures could be taken to improve the eugenics stock of Great Britain. For example, providing child allowances so that

the right sort of person would in fact have children, to encourage not just the working classes, but also the middle classes to have large families.

GLENDA JACKSON

Music
scd 130
Tr18 42"

Still: Fisher c Mrs Horace Norton

Whatever we think about Fisher's views on eugenics, some aspects of his hopes for the future are remarkably close to our own. After a lifetime of measuring the un-measurable, it's only now that his vision is able to become a reality.

ALAN GEFEN

Just as nowadays with the Genome Project there's the idea that we're on the brink of a new era in which we'll be able to use genetics to improve the human condition, Fisher believed that then.

ANTHONY EDWARDS

He was the first person to suggest when he was Professor of Genetics in London that if only we could develop a linkage map of man, it might be useful for disease prognosis, and in that sense he and his colleagues at University College in the 1930's are the parents of the Human Genome project.

GLENDA JACKSON

Music
kpm 362
Tr3
1' 53"

Still: Fisher and Joan c. J Box

Fisher died in 1962. But he had foreseen the far-reaching potential of combining statistics and genetics in the search for certainty. It's this creative synthesis, which proved most fruitful during his time at Rothamsted, that carries on today.

RICHARD DURBIN

I feel tremendously privileged to be involved in sequencing the Human Genome and I think everyone who works as part of the project feels the same way. Just as Rothamsted was at the

cutting edge of collecting genetic data in the 1920s and 1930s, the Sanger Centre is at the cutting edge of collecting genetic data now in the new millennium. We know we're producing something that is going to be a foundation for biological science from now on, for the next thousand years and five thousand years.

GLENDA JACKSON
From a deep understanding of who we are to the way we live our lives, statistics has a crucial role in our future, thanks in large part to the work of RA Fisher.

STEPHEN SENN
Fisher could hardly have dreamt how his ideas would be used today.

ALAN GEFEN
His influence is so pervasive that everything you do in statistics and everything you do in evolutionary biology can really be said to be Fisherian.

JOAN BOX
He was a genius of course, he followed his own bent.

Credits
We wish to thank
Antony Barrington-Brown
Norman Draper
Cambridge University Department of Genetics
Cambridge University Library
The Fisher Memorial Trust
Gonville and Caius College, Cambridge
Roger Payne
Gavin Ross

Narrator
Glenda Jackson

Academic Consultant
Chris Jones

Production Assistant
Sandra Budin

Production Manager
Ione Mako

Researchers
Irene Toxpeus
Helen Foot
Marinella Nicolson

Rostrum
Ken Morse

Camera
Colin Clarke
Sean Leslie

Sound
Tim White
Doug Dreger
Geoff Price

Dubbing Mixer
Trevor Barber

Editor
John Hackney

Series Producer
Stephen Evanson

Producer
Liz Gray