LIFE AND DEATH **Iona Heath**

The problem of diagnosis

The notion of lifestyle diseases allows the diagnoses we give our patients to excuse social injustice

Medicine urgently needs a broader approach to diagnosis: one that reveals more of the true causes of disease. As we slowly unravel the complexity of psychoneuroimmunology, we understand more of the extent to which the biology common to all human beings is modulated by the biography unique to each one. Yet the evidence on which clinical medicine is based remains rooted in generalisations derived from randomised controlled trials, from which every trace of individual difference has been deliberately excluded.

The problem is that human beings are not simply passive consumers of disease and injury. The first person to point out the fundamental significance of the meanings that animals, including humans, attach to their environment and experience was the Estonian zoologist Jakob von Uexküll (1864-1944). He argued that each individual was the result firstly of modification undergone by the species during evolution but secondly, and at least as importantly, of adaptation occurring within the individual during the course of each particular life. The evolutionary resources of the individual, including its genetic make-up, are modified by individual, subjective interpretations of life experiences, especially during early life. The meanings attached to these experiences alter epigenetic expression, so that various forms of trauma and stress have a profound effect on the individual's physiology. The response may turn out to be usefully adaptive, transitorily dysfunctional, or maladaptive.[1]

We are slowly beginning to understand some of the mechanisms in play. One concerns the epigenetic regulation of telomeres. Chronic stress damages and erodes telomeres and by this means seems to precipitate premature ageing in the individuals affected. Telomeres shorten with age in all replicating somatic cells. Thus, telomere length can serve as a biomarker of a cell's biological (versus chronological) "age."[2] The association between chronic stress and shortened telomeres has been shown for, among other people, those caring for people with Alzheimer's disease, mothers looking after chronically sick children, and women exposed to intimate partner violence.

Another mechanism plays out in the remarkable relationship between humans and microbes. It is becoming increasingly clear that the viruses and bacteria to which human beings play host assume a crucial role in the development of infant neuroimmunology. It has long been a medical convention to see microbes as external enemies, but this is no longer sustainable. In the adult human body bacterial cells outnumber human cells by a factor of 10 to 1. Mitochondria are bacterial symbionts within each human cell, and the human genome is littered with sequences derived from microbes. The vast colony of bacteria in the human gut, their associated viral bacteriophages, and the genetic resources available from this diverse array of microbes shape human metabolic and immune systems and contribute to the maladaptations that lead to diabetes, obesity, and inflammatory diseases.

Clearly, much more needs to be understood. Since the 1970s von Uexküll's ideas have been enthusiastically taken up and explored by biosemioticians, phenomenologists, immunologists, and neurophysiologists, but clinical medicine seems to be lagging. Soon it will no longer be possible to relegate the biographical experience of the patient to irrelevance and to discount the terrible consequences for health of structural violence within society. GPs and public health doctors should be leading the application of this knowledge to healthcare systems: the first group because continuity of care throughout the life course is a founding and defining characteristic of general practice, and the second because their preventive efforts seem increasingly misdirected.

"Sooner rather than later it will no longer be possible to relegate the biographical experience of the patient to irrelevance and to discount the terrible consequences for health of structural violence within society"

The medical anthropologist Nancy Scheper-Hughes defined structural violence as "violence that is permissible, even encouraged. It refers to the invisible social machinery of inequality that reproduces social relations of exclusion and marginalization . . . Structural violence 'naturalises' poverty, sickness, hunger, and premature death, erasing their social and political origins so that they are taken for granted and no one is held accountable except the poor themselves."[3] These processes are exactly those played out as health inequality in our society. The sociopolitical origins of the lack of hope and opportunity that leads to chronic psychological stress and to damaged physiology and premature death have been successfully erased by the pervasive notion of lifestyle diseases and associated risk factors—and no one is held accountable but the poor themselves.

The key skill of all doctors is diagnosis. However, diagnosis itself poses profound problems of scope and usefulness. Every experienced clinician is fully aware that no two people ever experience the same diagnosed disease in exactly the same way, and yet the taxonomies of diagnosis and the international classifications that underpin them ignore this underlying truth. The diagnoses tabulated in this way are theoretical abstractions, but we are inclined to give them a level of credence and reality that tends to exceed that granted to the patients so labelled. In this way, our diagnoses begin to condone structural violence and to excuse social injustice.

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References are in the version on bmj.com.
Cite this as: *BMJ* 2012;345:e6595

MEDICINE AND THE MEDIA

A show trial

Channel 4 missed a golden opportunity to educate the public about how science is done, says **Margaret McCartney**, with its pair of programmes showing a scientific study of the illegal clubbing drug MDMA

The drum roll that Channel 4 sounded for *Drugs Live: The Ecstasy Trial*, its "ecstasy on television trial," meant that even before its two programmes were screened (10 pm, 26 and 27 September 2012) the camps for and against had formed in the printed media. Channel 4 said that it was the "first experiment of its kind" to use functional magnetic resonance imaging (fMRI) to examine the effects of the illegal recreational drug MDMA (ecstasy) on healthy volunteers.[1] David Nutt, sacked from being a senior drugs adviser to the government over his stance on drug taking and risk, told the *Observer* that the project had two purposes: to "show the whole process—from design to analysis—of a scientific experiment being performed"; and to perform the imaging.[2] The Medical Research Council had turned down the request to fund the study. Nutt said that the study had scored highly but didn't fit with the council's portfolio of research, so Channel 4 stumped up the cash. Nutt said that he should "be commended for finding a way to do quality science." But was it quality science?

There are many concerns that the public is not properly informed about clinical trials and yet there is a clear need to reduce uncertainties about treatment. Throughout the programme, we were reminded that MDMA was controversial and that half a million people use it in the United Kingdom every year, and no one knows how it works or what therapeutic benefit it might have. *Drugs Live* was filmed with a studio audience, who stood to applaud, and this was broadcast live. Footage of the participants taking either MDMA or placebo was prerecorded. This was not a random selection of people; they included the novelist Lionel Shriver and a former SAS soldier.

Drugs Live lacked a description of how and why the trial had been designed. The key to quality research is first to review current knowledge, and if the show's intent was to show the public good science then this should have been demonstrated. The need for a placebo was not explained. In fact, the actor Keith Allen, another study participant, asked whether the effects that another participant described could have been because of placebo, the only person on the show to do so.

The fMRI results were explained by the presenter Jon Snow and Nutt, in conjunction with a giant plastic brain with parts that lit up to show when they were being "activated." The results from psychology experiments during and after the fMRI scanning were presented with unclear graphs and no sense of statistical significance or explanations of how the data would then be assessed. It fell to Evan Harris, the Liberal Democrat politician and another study participant, to explain that data should be written up, statistically analysed, peer reviewed, and published before conclusions could be drawn. Unfortunately, his explanations were given little priority in relation to the competition.

Viewers' tweets with their opinions about taking ecstasy were read out, and audience members explained their good and bad experiences. One trial participant thought she had been able to deal with post-traumatic stress because of the MDMA she took in the trial. Video footage showed a US woman who thought that using ecstasy together with psychotherapy had helped her deal with post-traumatic stress disorder. She told the cameras this because she wanted to "help lots of people."

Unusual camera angles and different screen colours were used often, presumably to hold viewers' attention, but they were a distraction. Some scientists argued that MDMA was an unpredictable and risky drug that was unlikely to be clinically useful; Nutt and his colleague Val Curran said the opposite. It was presented as a debate; yet it was unclear what was broadly agreed and what was controversial. Snow told us that the results were amazing and incredible; another presenter, Christian Jessen, collected vox pops from the studio audience and advised viewers on how to take ecstasy if they were determined to do so.

We rightly talk about drug companies having undue influence over clinical trials—but what about television companies?

Presenters Jon Snow and Christian Jessen: relied on vox pops and a plastic illuminated brain

We rightly talk about drug companies having undue influence over clinical trials, their results, and their presentation—but what about television companies? Channel 4's need to create the programme drove its description of the trial and presentation of the data. Had the methods and results been ascribed more importance, it would have helped the viewer appreciate the importance of randomised controlled trials as opposed to the power of anecdote. The live format promoted sharing of opinions, but the hierarchy of evidence was not explained or investigated. Originally the programme makers wanted to show the taking of ecstasy live, but a condition of trial approval was that it was not live. Making the remainder of the programme live seemed unnecessary.

Crucially, *Drugs Live* failed to distinguish clearly between the issues about illegal use of recreational drugs and the vast difference with the controlled clinical experiment being run. Viewers calling in often discussed personal experiences after illegal use of ecstasy. Many drugs can be misused but can also be prescribed and have clinical usefulness. There should be no difference if MDMA is found to be effective in some conditions, in which case there should be no stigma about using it. It requires a Home Office licence to study MDMA, and Nutt, explaining the current research situation to the *Observer*, said that drug companies were concerned about the potential for negative publicity should they research MDMA.

What MDMA could be effective for, however, has not been shown; and although the presenters described the fMRI findings of MDMA's effects as "groundbreaking," they neglected to tell us what this means for future research: statistics, more trials, more tests, and more questions. The relation between the fMRI findings and real life outcomes was not described; a researcher told one blinded participant that he thought she probably had taken the active drug. Nor was it clear what questions this trial could not answer, such as that it could not reassure people thinking about taking, or already taking, MDMA. It's necessary that the public engage with and understand science, uncertainty, and the need for clinical research, and how science works. But this programme was not an example of how to do so.

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References are in the version on bmj.com.

Cite this as: *BMJ* 2012;345:e6621