



# The New Pharmacology:

*Are tailor-made drugs changing health care?*

**Anders Sandberg**

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### **About the Speaker**

Anders Sandberg is Science Director for the Swedish think tank, Eudoxa, and co-author of *The New Pharmacology*.

Dr Sanders has a background in Computer Science and Psychology. He is an expert in artificial neural networks and in general health policy. He combines his knowledge of natural sciences with liberal arts in order to explain the emerging technologies and their consequences.

He regularly writes and lectures both in Sweden and abroad.

For more information please see: <http://www.eudoxa.se>

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Really what is happening right now is that we are seeing a kind of revolution in how we manage medicine. Part of this revolution comes from the fact that we understand our bodies much better. But other parts of it are technological – we are much better at learning things about our bodies, both as individuals and as a species. We are also getting better at creating new drugs. We are also seeing social and cultural changes.

These all mesh into each other, and this is creating an interesting setting where scientific results have political repercussions which, in turn, might be guided ideologically.

But to start out, I'm going to give some examples of what is going on.

In general, predicting the future is rather messy, and rather difficult. So I'm not going to try to do a prediction of "what are we going to eat ten years from now" or something like that – but rather to point out some different trends we are seeing and to discuss how they might interact.

One of the big trends we are seeing these days is pharmacogenomics. Genomics – that is something that happened when we combined genetics – modern methods of sequencing genes in particular with computers – together, these combined to create something much greater than the sum of their parts. The reason for this is that modern scientific methods create enormous amounts of data; computers are good at processing data. So what we're seeing is kind of a "brute force" science: Rather than

trying to use all of our brainpower to figure out “what this little thing is doing here with that little thing”, we let the computer do it, much more stupidly, but the computer analyses a hundred interactions – and then we can use our brains to figure out, *ah, which one of these is important and interesting?*

So, we are getting through enormous amounts of data, which is stimulating a lot of work in computer science and genetics. And we see that most drugs interact with our genetic inheritance. As a rule of thumb, when people ask you, *how much of this is genetic and how much of it is environmental?*, you can say 50 per cent, and that’s usually about right for almost anything. This holds true for quite a number of diseases and drugs – which means it’s important to understand how they interact.

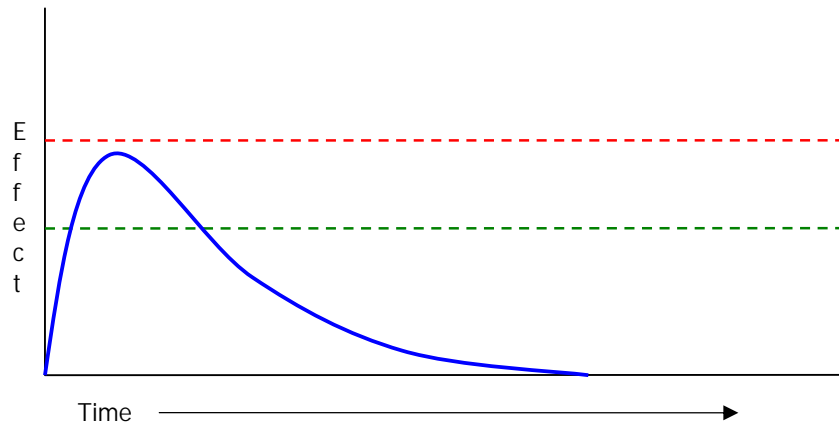
This has its origins in the 1950s when, during the Korean War, American soldiers received anti-malaria medicine. Approximately ten per cent of the African-American soldiers got anaemia and got seriously sick. It turned out that they actually had a different version of the gene encoding an enzyme that broke down the drug, resulting in these side effects. And this was the start of pharmacogenetics.

From the start [referring to slide], well, here is a chart showing the number of publications on pharmacogenetics from the 1960s to the present [the chart shows a gradual increase from the 1960s to mid 1990s, and then a sharp increase from the mid 1990s to the present]. People did pretty well in the 1970s, but it was really hard work: If you suspected that some drug interacted in some strange way with some group of people, you had to gather a large group of these people; you had to compare their genetic backgrounds (which required a great deal of difficult lab work that kept a great number of graduate students working hard).

What happened in the 1990s is that we got tools that suddenly made this work much easier. People started to realize, *oh this is great. We can perhaps use this for drug development. We might create personalised medicine.* That was the initial vision. Ideally, you would go to your doctor if you had a certain disease; he would take a genetic sample and then create a medication just for you. This initial vision has not quite come true, and it might not come true for a very long time.

But in general, the goal is getting the right drug, at the right dosage, to the right person. It might turn out that the right drug for me is not the right drug for you – or that we might need to change the amount of the dosage.

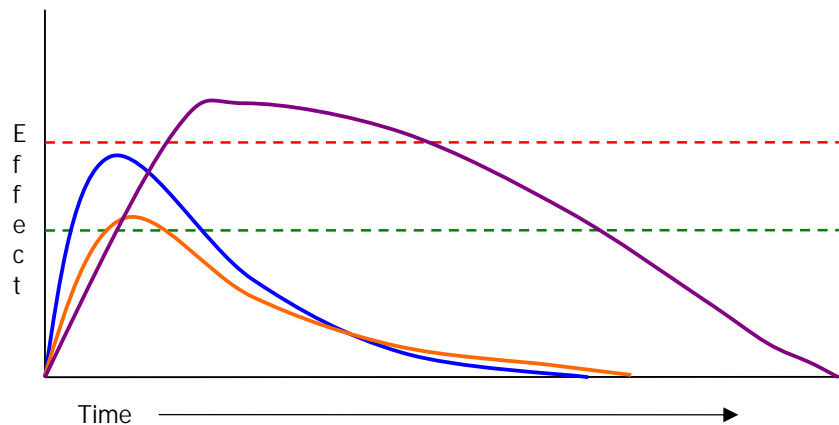
Here is a simple example [referring to slide below]. I don’t know if you really can see it, but just imagine the diagram anyway. (Suggestion is wonderful; it really helps you see what the person behind the lectern wants you to see.) This is a small simulation I’ve made of an imaginary drug. The blue curve is the amount of a drug you find in the bloodstream. So you take a pill or injection of it, it increases, and then it starts to decline after a while as the body gets rid of it.



Above the green line, this drug has some good effect – it might be a pain killer, for example. Above the red line, it has a deleterious effect. In the case above, we have a nice case in which there is a period during which the drug works, and then it doesn't work. So, your doctor tells you to take a pill every four hours or so in an effort to keep the level in the range between the red and green lines [between the dotted lines]. If you're "normal", then this is going to work well.

But imagine that you actually get rid of the drug more quickly [see orange line on chart below], and in this example you experience a very short period of very weak pain relief, and then it doesn't work. So even if you followed your doctor's prescription – and most patients don't really follow them very well...

(There is a both wonderful and really horrible area called "patient compliance" where people have been trying to figure out how to force patients to obey. It's really kind of "medical fascism" although it is, of course, as always, with good intentions. I personally think we have to find some good incentives to motivate the patients instead of forcing them. But anyway...)



This [orange] patient – the drug won't do much good for him. On the other hand, this patient [violet, above] is really going to get into trouble. His body is removing the drug at half the speed of the “normal” person. He immediately shoots up into the dangerous area above the red line and stays there for a long time. If he follows the doctor's prescription, it's not going to be good.

The cause of this can quite often be pure genetics. I don't know how much genetic and biology background you want me to give you – I can give a lecture about that, too, and it's rather fun. Actually, just tell me what you want to hear and I can go into it.

The important part here in general is that along the DNA spiral that carries our genome, our genes, there are codes for different proteins that the body makes, and these proteins then do different operations – like, for example, removing drugs. But they exist in different variants. We get these variants from our parents, and sometimes we have a mutation that creates a new variant. Each of us has about one individually unique mutation and then a lot of perhaps rare variants we might have inherited. And some of these of course affect how quickly we get rid of the drug. Some genes are extremely important in this respect. There is, for example, Cytochromoxidase P450, which is not only a real tongue-twister but is also extremely important because practically all psychiatric drugs (and quite a few others) are broken down by it; there are some quite large variations in how efficient it is. This is, of course, a big problem, because a depressed patient who gets a drug from a doctor tries a certain amount of drug; after a few months, does the patient get better, or does the drug have some side effects? If it has, well, let's change the dosage. It takes a long time and, if you're depressed, you're not going to get happier by that – and the problem is, of course, that up until recently there was no real way of finding out (for the doctor) what kind of patient you were.

Actually, adverse drug reactions are a huge problem – there are these scary numbers saying that about 100,000 patients die each year as a result of adverse drug reactions. And that 2.2 million Americans per year get sick enough to be hospitalised for it. The numbers are a bit iffy – it’s always hard to tell. But in general it’s far too large, the number, and it’s actually rather scary. We want to get healthier from the drugs, not to get more sick.

If we have this population where different people react differently, then there is no such thing as a normal dose; it’s just a “normal” dose that most “normal” people react well to. And the others? Well, there are a few who do not complain loudly; thanks to pharmacogenomics we can find them and give them different dosages, different drugs, or another means of fixing the problem.

This is also interesting: When one starts considering, for example, the cost of developing drugs... If you can screen a patient group, you can find the patients that react well to a drug – and that means that a drug that would have otherwise been removed from the market due to the fact that some people experienced side effects... Well, if you can warn against these side effects on the packaging and test them, then you can still use it. You can also use more genetically homogeneous samples when you develop the drug to get rid of some variations, get a more predictable result and show that *at least for this group of patients, it’s going to work well*. It makes it much easier to get the drug approved.

Overall, this long pipeline – I guess it is something quite a few of you are familiar with – the drug pipeline is too long. Things get stuck inside it. It’s getting slow and expensive. The problem is really that inventing a new idea that could be used for drugs... that’s really simple. It’s also fairly simple to do preliminary testing. But once you start doing the careful testing on real, live humans, the price goes up enormously and it takes a long time.

For an ordinary drug, it’s about 13 years, and it costs a lot of money. In the end it’s a huge gamble because some regulator might decide, *Oh, I don’t like the look of your drug. Do it all over again. Another billion dollars, please*. Hopefully, we could change these things with pharmacogenomics.

This is really an area where pharmacogenomics have demonstrated the most usefulness: We can screen for these toxic effects and find out which patients should and should not take this drug. We have some examples like the cancer medication Herceptin; it works against certain kinds of tumours but not others.

This was also a demonstration of how regulation can complicate things too much. The FDA wanted especially to check out the genetic tests that came with the drug. There was a lot of debate over, *should they be tested separately or do you deal with it as a package?* And that regulatory uncertainty, of course, scared a lot of other people. So far, there are only about three or four drugs that can be said to be purely pharmacogenomic. On the other hand, we have about twenty drugs that now have labelling telling that *certain patients will not react to this drug* or that certain patients

would react badly to it. There is, for example, a medicine against child leukaemia in which the drug, in about ten per cent of cases, causes really toxic side effects. The nice thing is that you really don't even have to do a genetic test – you can just do a blood sample test to discover a sign that *this patient breaks it down slowly, he should be taking a dose that is one-tenth of the normal dosage*. In that case it works wonderfully well.

Overall, what is happening is that these gene tests are getting smaller and they're getting cheaper. We're getting these wonderful DNA arrays. This one [referring to slide showing a genetic array] tells what kind of cytochromoxidase you have. So far they are not very well used in the medical profession; there is a need for education here to get them out – after all, doctors have plenty of problems already, and now they're having to find out the genetics of their patients. On the plus side, these screenings are getting much, much cheaper and much faster. In a few years, this will be something you can connect through your Palm Pilot. Quite a few people who discuss this tend to ignore that we are seeing something like Moore's Law here. It turns out that the developments we see in computer science seem to be mirrored for us by the ability for us to screen things. I don't want to bother you with the details of this but there's a wonderful paper that says essentially that we are going to end up seeing "gene hackers", because it's going to be so cheap to do gene testing and gene sequencing – it's bound to hit the streets. There are already people doing it completely outside the traditional borders of institutions. It's going to upset a lot of people.

The most important thing is that *patients are going to be able to get genetic testing*. Very cheaply. Probably over the Internet; we already see some of these services being sold. And it's not going to be under the control of the traditional medical institutions. Let's continue.

Overall, the promise of pharmacogenomics has been the usual: At first, people expect everything to happen at once. It doesn't. And then people think, *Oh, it's just a 'continuous development' thing. It's nothing new*. And so then they end up surprised after all. So we have to prepare these "rocket-engined snails" [referring to graphic drawing of giant snail equipped with futuristic rocket pack] that seem to creep up all of the time.

Then we have neuropharmacology, which is my favourite subject; I could go on for hours. Here is a simple example [referring to slide] showing the areas of a cat's brain and how they are connected to each other. A human has about four times as many areas, but it's the same kind of mess. The interesting thing is that we are actually getting pretty good at understanding this mess. We are not at the point yet where we can explain everything, but at least some of the interactions are starting to make sense, and there are some very interesting drug applications here. After all, mental diseases are costing society enormous amounts of money, and now we're starting to get past this idea that either a) you will lie down on the couch and listen to your psychiatrist or b) you will take a pill.

Actually, it turns out that it is much better to take a pill *while on the couch*. If I'm depressed I take a Prozac and I get better; the same goes for talking to a good therapist. On the other hand, two years afterwards, I am more likely to be depressed if I had taken only Prozac and then stopped than if I had taken therapy. The reason is, one learns coping strategies in therapy. On the other hand it's rather hard to teach coping strategies to a depressed person – he doesn't want to listen; everything is so bad. Give him Prozac and he will listen, and now he gets coping strategies, which means he's going to get happier much more efficiently. This is of course slowly, slowly breaking down a lot of the professional boundaries. It's going to be hard work. At least in Sweden, there is trench warfare between the traditionalists on both sides – they don't want to listen to each other, don't want to hear that there is something on the other side.

But this is changing in very interesting ways. Here is another example: memory enhancement. This [referring to photo of mouse] is a memory-enhanced mouse. It was genetically modified to express a gene that makes it learn like it was a young mouse all of its life. So it learns much faster but it is also somewhat more sensitive to pain, because it also uses that receptor for pain reception – so that's a slight drawback. On the other hand we might consider, *well, there is aspirin, and I want to learn more*. We might not do it by genetic modification, but there are other drugs that do affect memory and they are getting onto the market – first as Alzheimer drugs, but also now, thanks to the medicalisation of aging, “Aging related cognitive impairment” as it is called. The interesting thing: these drugs work for young people too.

And you can actually use them to treat phobias. A phobia is really a mis-learning. I learned that something is awful and dangerous, so I react extremely badly to it even if it is not very dangerous. If I'm afraid of mice, I'm going to cringe when I see that picture. The traditional treatment for this is to make me look at pictures of mice, then gradually stuffed mice, and finally I would get to holding a little mouse in my hand. This works fairly well; it's a good therapy. Unfortunately, if I get scared by a car accident in the meantime, I'm back to square one. It turns out that, due to the organisation of the memory system, my unlearning is – well, realising that I'm learning to ignore my previous fear. But using a memory enhancer during this therapy – people at Emory University have demonstrated that they can actually get rid of this problem of going back to square one. So here have a drug helping a therapeutic mental process.

The interesting thing is that this also opens the door to enhancing medicine. Once upon a time, most medicine didn't do anything. Then there were a few that helped with things like helping us with our pain. Then we finally got a few that started to cure things. Gradually we got much better at the curing of diseases. And we're also very interested in preventing diseases, because that's going to save society and ourselves a lot of cost.

But where is the line between preventing disease and enhancing performance? In sports, this is getting more and more complex, especially because a lot of ordinary

people who do sports take drugs and treatments that the professional athletes are not allowed to use. In 50 years' time, if the athletes are still going to be "un-enhanced" as they are today, they are going to be much weaker than the pensioners and other people sitting around watching them.

The interesting thing here is that "lifestyle medicine" has a bad ring to it – *oh, it's something people should pay for themselves*. On the other hand we have accepted, for example, The Pill, which doesn't really treat any medical condition. But it helps to support a lifestyle. It has changed how society works to a large extent. We are increasingly accepting the taking of Viagra and other stuff that makes us function better. After all, we want to live life to its fullest. And even if a few rare purists will say *no, I will not enhance myself*, quite a few are going to do it.

This is putting a lot of interesting pressure on doctors. Modafinil is a drug that is intended to work against narcolepsy – suddenly falling asleep. Suddenly, all of Silicon Valley has declared that it suffers from narcolepsy, and they are eating Modafinil like crazy. Probably it's going to drive a second dot-com boom, because, well... it's a stimulant, but it doesn't have these really dangerous side effects you find with traditional stimulants like amphetamines. Modafinil doesn't seem that addictive, nor does it seem to have that many side effects – except, of course, that people don't sleep very much while using it (which, from a memory point of view is not very good). But it seems there is a huge, very positive demand for this.

Then of course, we have the issue of doping in the Fine Arts. Quite a few concert musicians take beta blockers to calm their nerves before performing. There have actually been some debates as to whether this improves the music itself; arts people disagree vehemently about this, but there is no question that it is a widespread practice. So what is happening is that we are seeing a very new market – and also, it is supporting people in their professional lives.

In the end, we might end up with medical problems here. We have to decide, what kind of things we're eating.

This goes for food, too. After all, quite a few of my friends drink wine and say *oh, it's full of lovely antioxidants*. These days, hardly anybody eats food because it tastes good. It's eaten because it contains antioxidants, or it might contain "good bacteria" that will make you happier, it might be life-extending thanks to various vitamins, or have anti-cancer compounds. People are trying to – well, the interesting thing is that these foods are not regulated as drugs, of course – but people are buying into it quite largely. On the other hand, if you really tried to make a functional food that had really strong effects, people would be a bit suspicious, because of course it would be a non-traditional food. And regulators would be all over it because *oh, it's a new compound* – which is a bit sad, because there is huge potential here with the idea of "eating yourself healthy".

As an example, why not take a vaccine from bananas? This idea has actually been implemented, I think, for potatoes with an anti-cholera vaccine. Geneticists spliced

part of the cholera bacterium into a potato; when people ate the potato, they got antibodies against cholera. This is, of course, wonderful for the third world, where people have also been working on doing things with bananas. I think bananas are a bad idea because they are easy to mix up, you can slip on the peel, and it takes a long time to grow them on trees – but that’s mostly a design issue. We can probably find some other vegetable that most people won’t normally eat to get the vaccines.

We are also seeing vaccines that not only prevent people from getting diseases but also helping them therapeutically while they have a disease. We are seeing ideas about vaccines against diabetes. We’re seeing vaccines against drug use – for example, people have been designing a vaccine that should attack the cocaine molecule. So if you take this vaccine, you will not get “high” while sniffing cocaine – which is, of course, intended to help in drug rehabilitation. And a few politicians are already thinking *oh, we should really use this on the population – and why haven’t you finished that nicotine vaccine?* It turns out that, unfortunately, nicotine molecules are too small to really make a vaccine against them; but people are trying.

This of course raises other interesting questions about Who gets to add What to our bodies. All of this adds up to a lot of interesting challenges:

The first one is, of course, business models. It would be wonderful for the drug companies if we could reduce drug development costs with this. But it might also split the market. Currently, for example, you have one market for asthma medication. But now, imagine that you find out that different genetic variations are responsible for different kinds of asthma. Suddenly, you’re going to have perhaps ten markets – and that means you will only be able to sell your particular drug to perhaps one of them. You then have a much smaller market, but your development costs might not be much cheaper. That’s not really a nice development from the perspective of a drug company.

You might also end up with a lot of “orphan” drugs. *Oh, that kind of asthma. Yes, we know how to treat it, but nobody wants to manufacture or test a drug against it, because there are only a hundred people suffering from it.* Current regulations about orphan drugs are directed against certain diseases which are small – not really small, but you have a common disease and then one rare version of it.

And then we have a privacy issue. Genetic testing is going to get really cheap, and most likely it’s going to be possible to do it privately. Which means that if I leave a hair behind, some of you might want to find out *how does Anders really react to that drug?* (Or, for that matter, other interesting genetic stuff that might be there.) So people are getting worried about genetic privacy, mostly in terms of genetic testing for diseases.

It’s not really likely that you’re going to lose your job because it turns out that you cannot take a certain kind of penicillin. It might be an issue in certain jobs, where you might not want to have people exposed to certain chemicals – for example in the chemical industry, but it’s not really an intensive problem.

People want to control their medical information, and they're getting louder about it. On the other hand, in these trials that are being done, about 80 per cent of the drug companies are keeping a lot of DNA stored after the testing, just in case – if there are side effects in a few years, they can go back to find out if one group of test subjects had a certain variation.

So this creates a problem of developing trust, because we need to be able to trust. But if I take a genetic test, I want to trust that this is not going to end up being used to my detriment at the insurance company. The drug company wants me to do genetic tests so they can sell drugs that suit my genetic profile. On the other hand, they don't want to manufacture that before other people are willing to test themselves. So here we see a need to bootstrap this, to get the trust sorted.

To some extent this is fairly easy to do. After all, regulators love regulating privacy. It's not really that hard to set up a privacy regime for this. The hard part might be changing it over time, because this field is going to develop quite a bit.

We also have the interesting problem that different ethnic groups have different incidences of these variations. So certain drugs are going to work better for African-Americans or Europeans or some other group, and this is going to be really problematic, especially in egalitarian health systems that claim *we're going to provide the same health care to everybody*.

For example, there is the drug BiDil, which was recently approved. It's a heart medicine that works only – or, at least, “works reliably” only for African-Americans. Of course a geneticist would say *there is no such thing as race, it's just genetic variations*. But certain genes are much more common in certain groups, and some groups of people are going to say *Oh, that's a drug for blacks. Why should “we” subsidize it?* So we're going to see some rather interesting – and probably rather misguided – debates about this.

This is a model [referring to slide] I made some time ago about how technology can change the health care system. Technology is not forcing us to do this or that, but it is enabling a lot of stuff. Hospitals might be pushed to create health care “teams” containing not just a doctor and a nurse, but also a computer scientist and a geneticist and an information visualiser. We are also seeing a lot of information technology enabling decentralised care – which is already putting a lot of organisational strain on traditional hospitals. We are also seeing this new pharmacology, which blurs the distinctions between different kinds of medicine – and this is supporting a new idea of health: *I'm healthy if I function as well as I want to, not if I'm functioning “normally” or like the textbooks say I should be functioning*.

If I want to sleep only four hours a night, I'm healthy if I can achieve that without any side effects. This is, of course, very different and it's really nothing that is possible within current funding systems. But we're seeing pressure in this direction because patients are increasingly thinking along these lines; they are in the corner

saying that the doctors – who tend to listen to their patients, though there is a slow change in perspective. We’re slowly going from the “patient as a client” (who has to obey the doctor) to more of a “customer” model – and that is what is going to speed everything up. We’re seeing a “feedback loop” here. We’re seeing an empowered patient who shows up at the doctor’s office with a genetic test and some printouts from the Internet; these patients are highly motivated. They have read up on their disease because it matters to them much more than it does to the doctor – to the doctor, well, it’s another customer. Or another patient. It’s just a problem. But the patient wants to get the best possible care, and this is creating enormous strain on the monopoly health care systems. This is where we are going to see really big battles in the future.

On the other hand, what can the regulators do? They cannot change culture. They can try to stop this trend, but I think it’s rather hard to prevent the empowerment of the patient. The problem is when we think in terms of cost minimisation we tend to think that *oh, the system is fixed. We should just reduce costs in some way.* And that is a problem because sometimes, we might want to change the system. To really minimise costs, we might have to do things differently.

So, in the end [slide showing Magritte’s *Golconde*], there are the regulators. They are raining down. What would Hayek do? I couldn’t find an image of him so I have chosen Asclepius instead. He’s a good stand-in. He would say that organisation and spontaneous order are both very important. What we’ve been seeing over recent years is that when it comes to the synergies of technology, who is the best at adopting them? It is actually the patient organisations. They do not have the enormous resources we see in the pharmaceutical industry, nor do they have the regulatory powers we see in the administration, but they do have the interest. They are very good at picking up communication through the Net, and they are also getting more and more involved in research.

One interesting possibility that might be worth considering is that they actually take part in doing some of the funding that funding agencies and the pharmaceutical corporations are not really interested in doing. Like, for example, doing genetic outcome trials for Warfarin – which has not been given much funding because it’s obvious that there is some effect so it’s not scientifically interesting, so the funding agencies won’t fund it. And it’s a generic drug, so most drug companies won’t fund it. But for patients at risk of stroke, for example, this is extremely important, and it might be possible to fund this more cheaply using genetic testing and the Internet.

It’s probably also important that we find ways of getting around how trials are made. Maybe we should open up trials more. We might actually have to trade some drug safety in order to get more drugs. We don’t want that drug pipeline closed when we really need a new drug.

Overall, I think Hayek would quote Hippocrates, who said *First, do no harm.* We shouldn’t harm development of the new pharmacology by regulating it too heavily. We should actually accept that this innovation really requires a lot of

experimentation, and that some of these drugs are going to have nasty side effects – but we are going to learn from that. Some of the drugs are going to have unexpected side effects, like that blood pressure medicine Viagra that turned out to be much more interesting than just a blood pressure medicine.

Quite often, we need to recognise that we cannot control this technological development. Instead, we should aim to guide its force toward the areas where we think it can do the most good. Thank you.

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## Q and A

Q: How do you think all of this new technology will affect the approval process for new treatments? Will it make things faster, or will it slow things down? Will approval committees know how to test them, or will changes be needed there, as well?

A: The development over the last century has essentially been that we want safer and safer drugs. Now, we're getting better and better at testing them so that we can be almost perfectly sure they are safe for everybody. The problem here is of course that it is making the drug pipeline longer and longer; it is harder and harder, slower and slower to get a new drug approved. It also often turns out that if there is some side effect for somebody, that you will have to withdraw that drug. This can be exceedingly costly as we have seen in the Vioxx case. So the problem might be that – well, we don't really want unsafe drugs; snake oil salesmen are dangerous to our health. On the other hand, for new drugs that are being developed, quite a few patients are willing to participate, and they are getting more and more organised. They are willing to extend their trust. But this kind of thing requires us to have new rules regarding how the trials are made, enabling the use of people who want to participate.

This can also be problematic from a purely scientific point of view, actually. In a scientific trial you don't really want self-selected patients, because they might be different somehow. There was a huge uproar in the Herceptin trials about this – in the end, actually, the company gave in; it allowed self-selected patients and has actually benefited quite a bit from it.

In the end, you might actually want to have a tiered safety regime. On one tier, here are some drugs that are, well, safe enough to be tested in a trial. In another group, here are some drugs that have been tested fairly well; we can't say we know everything about them, but... And then of course the group like we have today, of drugs we know everything there is to know about them.

This is a large change and I don't think it will happen overnight. But I think the trend toward personalised medicine is moving toward this. There will be a huge resistance to this, because we have an enormous administration based on the current system. Even the drug industry has to change a lot, too.

Q: One aspect of this that you touched upon was that today, medical doctors often know less about patients' illnesses than the patients themselves – because, as you mentioned, the patient has a greater interest to get into the details. Well, another aspect of this might be this: If you are a medical doctor in the traditional system, you can basically prescribe any drug to anyone. But with this development, it seems probable that we will see that really, well, non-specialist medical doctors will not be trusted to make the right decisions when we have more and more complicated drugs – drugs that should be delivered in combinations with therapy or perhaps to specific genetic profiles. Do you think we will see a challenge to the way doctors prescribe medicine today?

A: I think this is already happening to some extent. On one hand, a pharmacogenomic drug should not be prescribed as openly as a traditional one. On the other hand, “patient power” means that patients are going to ask for a lot more labelling of prescriptions. This is probably going to be one of the hottest struggles in the next years.

Q: With regard to the ever-longer pipeline the pharmaceutical companies are facing with new drugs, is there any possibility drug companies might use some of this technology to speed up the development or otherwise reduce costs when, as you say, they might be developing drugs for smaller and smaller markets?

A: It might be interesting if we left the “manufacturing” approach to drugs and made it more of a “craft” instead – though this is not what a pharmaceutical company would want. But interestingly enough, some biotechnology companies might be able to squeeze into the market, because their techniques might work well in developing very small and narrow drugs. It might actually be that we are going to see – something like how Apple Computer got into the music business, to the great surprise of all of the music industry actors. After all, they are a computer manufacturer, but they were able to squeeze into a different business by means of a new technology.

Q: If and when insurance companies are allowed to see the genetic data of their customers, what do you see as the dangers?

A: This is a really problematic area, because current regulations say that insurance companies are not really allowed to look at this data. That's unlikely to change over the next years. However, patients are going to be very interested in using the information they have about their own genetic abilities and risks – which

means that they will have an “information advantage” over the insurance companies. Will this be an “insurance company killer” or not? I don’t know. For certain diseases it might actually be very significant. On the other hand, knowing I have a predisposition for, say, Alzheimer’s – it doesn’t really seem to be significant enough to break the companies if some people choose to buy shorter-term life insurance based on this information.

The other view is that the insurance companies are going to test us all and that people with anything perceived as a genetic “defect” will be refused insurance – which is rather unlikely in a free market. After all, in a purely free market, quite a few genetic variations are completely acceptable – this can be managed.

Perhaps the solution is another form of insurance: gene insurance. When, as a parent, I’m going to have a child, I’m going to get some gene insurance for that child, and this insurance will cover the cost of accidentally having some very bad genes. In most cases, of course, it’s not going to happen, so this insurance company will make a tidy profit. That is a completely free market solution to this problem.

Q: I think the area between medication and food will be more blurred in the near future. When you talk about food in the future, you should also move more in the direction of “nutri-ceuticals”. On one side, we think we have more choices than ever before, but in reality we have far less choices than we had in the past. Biodiversity has shrunk enormously. If you look at vitamin content of products, it has shrunk over the past decade, sometimes by as much as 70 percent per product. If you look at young people now, on average only about two per cent of them get the daily requirement of vegetables, and seven per cent get the needed amount of fruit. So I think it’s important to remember that if you want to prevent disease, it would be good to strengthen people’s immune and resistance systems.

A: Those are very insightful comments. I disagree a bit about the link between biodiversity and vitamin content. What has really been happening is that people have been designing foods in terms of shelf life, storage, appearance and other factors. Up until very recently, nutritional content has not really been a high priority. What is happening now is that it is becoming a high priority. In ordinary food stores, you now see products boasting of their nutritional content. The problem is really that some groups are taking this to heart and eating very nutritiously, while young children are not so interested in this content. There is a “food” culture and a “health” culture, and this presents an important challenge to the current system, because we are going to have a very health-aware older generation, and then a split between “health-aware”, “non-health-aware”, “differently health-aware” and other sub-groups.

But overall, I think we can certainly improve our health by improving our food; there is great potential here.

Q: About “orphan” drugs, do you think the free market will offer a solution somehow? You said that for some of these drugs, companies don’t see any profits in pursuing such small markets (or small numbers of patients). So what is the solution?

A: I think the best way to make this happen would be to lower the thresholds of drug research – primarily by reducing regulatory costs, which are really horrendous.

Another possibility might be that we change the way we do some drug trials. People who need orphan drugs are, in general, much more motivated toward participating in trials. One can also imagine that from the perspective of insurers, orphan drug development might be worth paying for.

So there are routes, but I think it is always going to be tricky if you need to develop something rather extensive for a small market. That’s really hard, but overall, the cost of drug development has been going down – it’s the marketing and regulatory costs that are increasing.

So in the long run, given technological development, it will certainly be easier to develop orphan drugs, even in smaller organisations – we just need to be sure that we don’t have to pay extra for that.

Q: A more political question. One political viewpoint might be: *This is crazy, it’s all unregulated, we need to regulate this*, whether it’s orphan drugs or genetic stuff or whatever. Within the scientific community developing these things, do you sense there is a split? Are there some people who, while pushing the boundaries of science, are on one side or the other? Or is there a political consensus among scientists?

A: I think scientists are always thinking *things would be better if we did this* – “this” being whatever they are currently working on. Unfortunately, most people are rather stuck in a statist view. When you work and live inside these organisations, be they large drug companies or regulatory agencies, the perspective – the horizon - is limited.

I think the change is going to come from the outside. I think the patient groups will be on the vanguard, forcing the change.

Q: A follow-up on orphan drugs. Where has the system failed, and can you expand further on how you see new and old players using what is in the public domain to move some of these drugs forward?

A: Again, I think you have to reduce the regulatory costs – that’s probably the only market-based mechanism that really works for it. On the other hand, we also see that the methods of developing and testing drugs – it will be much easier to do this testing in a few years, thanks to technology. Using the Internet, it is possible to put together data in real time from patient populations.

So far it's mostly science fiction, but one could imagine that a patient could take a genetic scan, they try the drug, then have computers storing general information about their environment, et cetera, and pulling all of this together into a data mine. The interesting thing is that there's nothing to say this has to be done in a corporate setting or by the state; it could become cheap enough to be done by a patient organisation. This is still many years off, but it is approaching faster than most people would expect.

Orphan drugs are a hard problem. Even if the government goes in and says, *oh okay, we're going to pay for it*, the government will always very quickly add that *well, we're not going to pay for everything* because they then realise it's going to be too expensive. They would agree to pay for certain orphans. So you still have the problem of market failure because the state really doesn't want its costs to go up, either.

It isn't going to be easy. I don't see a good, practical, easy solution to this problem.

Q: What about pharmacoeconomics (the study of the cost-benefit ratios of drugs with other therapies)? How does that fit into all of this? Have any efforts been made to demonstrate the cost effectiveness of this new pharmacology?

A: That sounds like a very interesting area, though I have not seen much on it myself and it is probably well worth looking up. One problem is that when you look at patients from a medical perspective, patients are simply a problem. A problem that costs money. Whoever you are, you must be paid for, and it would be so much better if you just went away. If we could just define you as "healthy" then everything would be fine.

And of course a new treatment, from the perspective of whoever is paying, *oh, it's going to be so costly*. Whenever I talk about new technology in a mixed audience, I can immediately recognise the Swedish politicians because they are the ones that start to look depressed when I begin to go on about all of these wonderful new methods, because they're thinking *oh, no, we have to pay for that, too?*

So once again, I don't really have a good answer, but I would say that technology generally reduces friction in systems. We're getting better at doing what we want – and this, in general, makes prices lower. Technology also makes it easier to detect side effects and things of that nature – and technology also helps us keep track of where the money is going. Quite a few of the old health care systems are extremely good at hiding – even from politicians and the oversight committees – where exactly all of the money ends up. In Sweden, where we have marvellous studies about everything, it is still almost impossible to answer the question *how much does health care cost?* You can find the "input" and the "output" but not what is happening inside the system.

So I think that technology might help us less through the biological pathway than through the pure information systems, allowing us to control where exactly the money goes.

Q: Following on the last question, I think you should really take the study of pharmacoeconomics on board into your further research; the link between “design medicine” and pharmacoeconomics is really an interesting area of research. If you look at the way pharmacoeconomics is used right now, it’s mostly to help the budget – not to help the patient or the GP. In Germany they have set up an entire administration to implement this idea, to prevent access to certain medicines, to reduce reimbursement levels. It touches on a bigger issue, which is choice in health care.

A: There is also the problem that you don’t see that you’re earning a lot by having a healthier population. After all, a slight increase in general health is an enormous source of revenue – but that shows up in a different account. So if you’re responsible for paying the costs of patients, you’re only going to see a cost. You’re not going to see the reward from that.

Q: If it means living longer, of course, it can be very costly for the government – here in Belgium right now we have this big debate over the pension age for people who work in the public sector. Anyway, my question is about enhancing or lifestyle drugs. Of course we are already seeing the cost side of this, as many government systems – as in Sweden – are not covering them. You have to pay for it yourself if you want it. I’d like it if you would speculate regarding the development of this type of drug. Where will we see the first major debate, not so much about the cost as about whether it is ethically okay to use them. I liked your description of the retirees potentially being stronger than the athletes, and I can see a lot of strong debate coming up on that. Where do you expect to see the first examples of this kind of debate?

A: Although there are treatments like enhancing regeneration – which would be really great for doping – that are going to appear in a few years, they are not going to be the source of the really big debates. The first really big debate is going to be some cognitive enhancement drug. It might even be over the widespread use of something that already exists, like Modafinil. Or it might be one of the new generation of memory enhancers intended to help middle aged people with a little bit of a memory problem, when it becomes widely used for youth. That’s probably where you get the flash point. People tend to be rather altruistic about health; we’re willing to spend quite a few of our euros on our fellow man to keep him healthy. But we don’t want to spend our euros making them better than healthy. I’ve seen evidence in studies that people’s altruism really stops at just getting people to normal. Which means people are going to react to memory and cognitive enhancers. This is especially threatening to many people – after all, if somebody gets healthier or stronger or more beautiful, that’s one thing. But smarter? That’s something eerie.

So, I think cognitive enhancers, in the next five years, are going to really cause a big debate. And of course some people might think *oh, if we could be a little bit smarter, how much more could Sweden earn in export money?* And on the EU level, *perhaps we might meet the Lisbon targets by getting smarter.*

Q: You have spoken a lot about patients increasingly being the keepers of medical information. How do you see this changing the relationships between doctors and patients and drug companies?

A: That's interesting, because if a patient owns his medical history, that's going to be an extremely valuable resource. It might be interesting for drug companies to buy parts of it from patients. And perhaps patient organisations can organise this. I haven't thought about it very much, except that patient-owned histories are going to be hard currency. This will be difficult for doctors, because as long as the doctor owns your information, you're really stuck with him regardless of what he does. But if you own it, you will have much more control over the kind of health care you are going to get. People are going to shop for their doctors much more. It seems entirely possible that people might wish to sell their medical histories.

To conclude, I think the goal should be that we are healthy and rich. And we're going to be rich because we're healthy.

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