Insulin Dependent Diabetes Trust
News Archive 2002

Doctors worried about threat to supplies of animal insulin

Mark Hunter, Leeds
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Fears that worldwide production of animal insulin could be put at risk by the proposed takeover of Brazilian manufacturer Biobras have been dismissed by the multinational pharmaceutical company involved in the buy-out.

Novo Nordisk has “no plans for the discontinuation of production of animal insulin.” Nor will it halt Biobras’s supply of source material to other companies that manufacture insulin, claimed Novo’s executive vice president, Lars Jorgensen.

Concerns over the bid, which has been accepted by the Biobras board and is currently under consideration by shareholders and the Brazilian competition authorities, have centred on Novo’s recent policy of scaling down its production of animal insulins. Its mixed porcine and bovine product Lentard was withdrawn from the UK market in July last year. In contrast, Biobras is one of the world’s major manufacturers of animal insulin and, significantly, one of the few remaining producers of the insulin crystals used by other companies as source material for their own animal insulin.

This has led some diabetic patient groups to fear a hidden agenda in Novo’s bid for the Brazilian company. “Novo have already stated their intention of global withdrawal of all animal insulins,” said Jenny Hirst, joint chair of the Insulin Dependent Diabetes Trust. “My concern

is that if Novo withdraw completely from the animal insulin market, they are not going to be interested in supplying anyone else with the source material."

This would be of serious concern to the significant minority of patients with type 1 diabetes who had been unable to switch to synthetic human insulin because of problems with intolerance or increased risk of hypoglycaemia, she said. Around 25 000 patients in the United Kingdom still use animal insulin. Ms Hirst also pointed out that many developing countries were unable to afford the higher priced synthetic insulin and would suffer greatly if Biobras ceased production of source material.

At CP Pharmaceuticals, the United Kingdom based company that is currently the only manufacturer still to produce both porcine and bovine insulins, the Novo bid for Biobras is being observed with great interest. However, the chief executive, Charles Savage, is keen to emphasise that although the company does have a "relationship with Biobras for the supply of crystals, there are other reliable sources."

Indeed the company has recently increased its production capabilities to step into the breach left by Novo Nordisk and Eli Lilly's gradual global withdrawal of animal insulins. "We are committed to the long term supply of animal insulins to the world's diabetics," said Mr Savage.

Doctors named as authors may not have seen raw data

The Guardian
Sarah Boseley, health editor
February 7, 2002

Marilynn Larkin is a self-employed writer and contributing editor to the Lancet, one of the most prestigious medical journals in Britain. While looking for work earlier in her career she agreed to ghostwrite a scientific paper for a medical communications agency retained by a drug company. It was her first and last incursion into that world.

"First I had to sign all kinds of forms not to tell anyone I was doing this," she said. "They gave you an outline, then provided tons of references you knew you had to use.
"I discovered I didn't like this kind of work. After I sent it, I got the whole thing back from the company with a sample from another company which read like PR writing. It was just a really straight sell. I said, 'I'm sorry, I can't do this.'"

The article was destined to be published in a medical journal supplement under the name of a research scientist. Ms Larkin says there are several kinds of scientists who will agree to have articles ghostwritten. "One is the person who has been around for centuries and is like a figurehead in the field. By that time, they don't care. They will take the money or pretend they didn't know they were taking the money for that reason. Or there are scientists who don't realise what is happening. They think they are getting help with writing and don't realise when they get feedback that the drug company is also going to review their work in most cases. There's no question that the drug company has the last say."

Many ghostwritten articles go into industry-sponsored supplements, she says, but many are published in the less prestigious medical journals themselves and "some of the ghostwritten articles go into top-tier journals", she says. "It is a pervasive problem with the whole medical publishing system."

In Ms Larkin's experience, the doctors who are supposed to check and approve the articles that go out under their names are not always assiduous about it. She once helped to edit a supplement based on talks given by research scientists at a symposium. "The writers did go back to the researchers to check the quotes for accuracy. More than half of the scientists did not get back to them ... They can't be

bothered to look at it or they don't care. I couldn't believe it."
Scientists are accepting large sums of money from drug companies to put their names to articles endorsing new medicines that they have not written - a growing practice that some fear is putting scientific integrity in jeopardy.

Ghostwriting has become widespread in such areas of medicine as cardiology and psychiatry, where drugs play a major role in treatment. Senior doctors, inevitably very busy, have become willing to "author" papers written for them by ghostwriters paid by drug companies.
Originally, ghostwriting was confined to medical journal supplements sponsored by the industry, but it can now be found in all the major journals in relevant fields. In some cases, it is alleged, the scientists named as authors will not have seen the raw data they are writing about - just tables compiled by company employees.

The doctors, who may also give a talk based on the paper to an audience of other doctors at a drug company-sponsored symposium, receive substantial sums of money. Fuller Torrey, executive director of the Stanley Foundation Research Programmes in Bethesda, Maryland, found in a survey that British psychiatrists were being paid around $2,000 (£1,400) a time for symposium talks, plus airfares and hotel accommodation, while Americans got about $3,000. Some payments ran as high as $5,000 or $10,000. "Some of us believe that the present system is approaching a high-class form of professional prostitution," he said.

Robin Murray, head of the division of psychological medicine at the Institute of Psychiatry in London, is one of those who has become increasingly concerned. "It is clear that we have a situation where, when an audience is listening to a well-known British psychiatrist, you recognise the stage where the audience is uncertain as to whether the psychiatrist really believes this or is saying it because they them selves or their department is getting some financial reward," he said. "I can think of a well-known British psychiatrist I met and I said, 'How are you?' He said, 'What day is it? I'm just working out what drug I'm supporting today.'"

Marcia Angell, former editor of the New England Journal of Medicine, wrote a year ago that when she ran a paper on antidepressant drug treatment, the authors' financial ties to the manufacturers - which the journal requires all contributors to declare - were so extensive that she had to run them on the website. She decided to commission an editorial about it and spoke to research psychiatrists, but "we found very few who did not have financial ties to drug companies that make antidepressants."

She wrote: "Researchers serve as consultants to companies whose products they are studying, join advisory boards and speakers' bureaus, enter into patent and royalty arrangements, agree to be the listed authors of articles ghostwritten by interested companies, promote drugs and devices at company-sponsored symposiums, and allow themselves to be plied with expensive gifts and trips to luxurious settings. Many also have equity interest in the companies."
In September her journal joined the Lancet and 11 others in denouncing the drug companies for imposing restrictions on the data to which scientists are given access in the clinical trials they fund. Some of the journals propose to demand a signed declaration that the papers scientists submit are their own.

The success of Prozac, the antidepressant which became a cult "happy" drug in the 1990s, substantially raised the stakes in psychiatry. Its promotion coincided with the decline of state funding for research, leaving scientists in all areas of medicine dependent on pharmaceutical companies to fund or commission their work. That in turn gave the industry unprecedented control over data and ended with research papers increasingly being drafted by company employees or commercial agencies.

The responsibility of scientists for the content of their papers takes on serious significance in the context of court cases in the US, where relatives of people who killed themselves and murdered others while on SSRIs (selective serotonin reuptake inhibitors) - the class of drug to which Prozac belongs - claimed the drugs were responsible. According to David Healy, a north Wales-based psychopharmacologist who has

given evidence for the families, the companies have relied on articles apparently authored by scientists who may in fact have not seen the raw data.
Dr Healy, who had unprecedented access to the data that the companies keep in their archives, said: “It may well be that 50% of the articles on drugs in the major journals across all areas of medicine are not written in a way that the average person in the street expects them to be authored.”

He cites the case brought last year against the former SmithKline Beecham (now GlaxoSmithKline) by relatives of Donald Schell. The court found that the company’s best-selling antidepressant, an SSRI called Seroxat, had caused Schell to murder his wife, daughter and granddaughter and commit suicide.

The company’s defence was based on scientific papers which analysed the results of trials comparing Seroxat with a placebo and found there was no increased risk of suicide for depressed people on Seroxat. But the raw data probably does not support that, argues Dr Healy. Some of the placebo suicides took place while patients were withdrawing from an older drug. When the figures are readjusted without these, he says, they show there is substantially increased risk of suicide on Seroxat.

This raises the question of whether the eminent scientists whose names were on the papers ever saw the raw data from the trials - or saw only tables compiled by company employees, he says. David Dunner, a professor at the University of Washington, who co-authored one of the papers in 1995, admits he did not see the raw data. “I don’t know who saw it. I did not,” he said. “My role in the paper was that the data were presented to us and we analysed it and wrote it up and wrote references.” His co-author Stuart Montgomery, then of St Mary’s hospital medical school in London, declined to answer calls and emails from the Guardian. The third name on the paper is that of Geoff Dunbar, a company employee.

The World Health Organisation has expressed concern about the ties between industry and researchers. Jonathan Quick, director of essential drugs and medicines policy, wrote in the latest WHO Bulletin: “If clinical trials become a commercial venture in which self-interest overrules public interest and desire overrules science, then the social contract which allows research on human subjects in return for medical advances is broken.”

Insulin inquiry urged - safety of synthetic product called into question

Toronto Star
Prithi Yelaja - Medical Reporter
February 7 2002

A group representing Canadian diabetics is calling for a public inquiry after uncovering reports of eight deaths and 465 adverse drug reactions linked to genetically engineered insulin. The Society for Diabetic Rights held a news conference in Ottawa yesterday and demanded that Health Canada ensure greater access to an older form of insulin derived from pork and beef. There have been only nine reports of adverse reactions to pork insulin, and none to beef insulin. The information on the deaths and adverse reactions was obtained under federal access to information law, said Colleen Fuller, the society’s spokesperson. “Over the last year, we’ve spoken to over 250 people across the country who have had serious problems with this type of insulin. The previous health minister, Allan Rock, swept our concerns completely under the rug.”

A Health Canada spokesman said that synthetic insulin products are as safe and effective as insulin from animal sources. “They have an excellent safety record with over 200,000 Canadians using them daily to manage their diabetes,” said Andrew Swift. Assuming patients take injections twice per day, there are 400,000 doses of synthetic insulin administered each day or 146 million doses per year, he added. The

synthetic insulin includes a product warning that some patients have reported the early warning symptoms of hypoglycemia, which occurs when blood glucose levels fall below normal, were less pronounced than for animal insulin, Swift said. However, “it’s hard to pinpoint... whether it’s the synthetic insulin that caused (these reactions) or some other factor.”

In the United States, there have been 92 reported deaths and 4,000 adverse reactions reported by diabetics using synthetic insulin, which was introduced in 1982. Although most diabetics can use it without a problem, the society says a significant minority experience serious reactions including hypoglycemia unawareness, convulsions, seizures and insulin shock.
“The effects of hypoglycemia and loss of warnings on the lives of some diabetics and their families can be enormous,” said Jon Hunt, a former head of the Canadian Diabetes Association.

Driver pleads guilty in teens’ crash deaths

LA Times
Gene Maddaus
March 5th 2002

RANCHO CUCAMONGA - A 48-year-old man will spend four months in jail and 2 1/2 years on electronic monitoring after pleading guilty Friday to three counts of vehicular manslaughter in a crash that killed three teenagers a year ago. Kristian Sid Aboy of Ontario will surrender to San Bernardino County jailers at his sentencing on March 22.

“My client was trying to show remorse and put this behind him,” attorney Gregory Kassel said in explaining the plea. Aboy was at the wheel of a car that ran a red light on Feb. 15, 2001, and broadsided a car carrying Brien Maloney, 14, Katie Nelson, 15, and Curtis Workman, 14. He was going 10 to 15 mph over the speed limit.

The teenagers’ families are upset that the law allowed prosecutors to file only misdemeanor charges in the case and are pressing lawmakers for tougher penalties in such situations. Aboy faced a maximum of three years in county jail, but Deputy Dist. Atty. Gregory Tavill said it was highly unlikely that he would be sentenced to the maximum if convicted at trial.
“This is a good disposition for us,” Tavill said. “It would not have gotten better for us, post-trial.”
Judge Gerard Brown worked out the plea deal, in which Aboy is technically sentenced to the maximum penalty, but will be allowed to serve the last 2 1/2 years at home. He will have to pay $450 per month for the electronic monitoring program. He will be allowed to go only to work and church, and gets four hours per week to go to the grocery store, probation officer Monica Cory said.

The families did not object to the outcome, but they were not happy about it, either.
“We’re not satisfied,” said Chris Workman, Curtis’ father. “But then again there’s no sentence that would satisfy us, as far as being equitable to the loss we felt.”

Aboy will also not be allowed to drive for the next three years. Kassel maintained that Aboy was in “a kind of comatose state” when he crashed his car, due to conflicting medications for diabetes and manic depression. “He should have been warned not to drive, and he wasn’t,” Kassel said.
Workman said the families agonized over whether by acquiescing to the plea agreement, they were not fighting hard enough for their children. “We’re still frustrated with it. We feel the judge maybe could have imposed a stricter sentence,” he said. “How bad a tragedy does it have to be?”

IDDT sent to following letter to the LA Times:
Driver pleads guilty to teens’ crash deaths
My sympathies go to the families of the teenagers killed in this tragedy and nothing can make up for their loss. However, I also extend

understanding to the driver of the vehicle, Kristian Sid Aboy, who was said to be in a comatose state when driving his vehicle. I have no doubt that this was due to hypoglycemia [low blood glucose levels] that occurred without any warning symptoms. This is a dangerous situation and no one should be driving under these circumstances. There have been similar cases in the UK and even a case of murder when this comatose condition occurred. In all the known cases the people have been using synthetic 'human' insulin which is known to cause loss of warning symptoms in some people. It has also been shown that in many cases a change to natural animal insulin results in the return of the warning signs enabling the person to take the remedial action of eating or drinking something sweet to raise the blood glucose levels.

There is a sub-group of people that are better treated with natural animal insulins. But all too often people with diabetes that are prescribed 'human' insulin are not told of the risks of hypoglycemia without warnings and nor are they told that this may be worse if they are using other medications. This case highlights the dangers for some people when using synthetic 'human' insulin and ignoring the known adverse reactions to it. I would suggest that some of the guilt rests with those who, for a long time, have ignored the reports from people with diabetes about the increased number of hypoglycemic attacks and loss of warnings with the use of synthetic 'human' insulin.

Jenny Hirst
Co-Chairman
Insulin Dependent Diabetes Trust

Synthetic insulin, a safer choice

The Times of India
Mar 7, 2002

BANGALORE: Synthetic insulin or natural insulin. Which one fares better when it comes to treatment of diabetes? Arguments and counter arguments, the debate goes on...

Unlike synthetic insulin, natural insulin cuts through the blood-brain barrier and gets into the brain causing major side effects including hypoglycemia, said Dr C.B. Sridhar, consulting professor of diabetes and endocrinology, St. John's Hospital, quoting a recent Wall Street Journal report. On the advantages of synthetic over natural, he said synthetic insulin is synthesised from human recombinant DNA and is more compatible to human body functions. Natural insulin is available for Rs 80 to Rs 120 per vial as against synthetic insulin at Rs 200 per vial. ``The research and development of synthetic insulin costs a lot,'' he said.

Synthetic insulin (human insulin) was introduced in 1980. Over 90 per cent of of the countries use this. Diabetes occurs when a human physiology fails to produce insulin or respond to the insulin produced by the body. This affects the blood sugar level and leads to a condition called diabetes mellitus. However, administration of insulin helps to maintain the normal blood sugar level.

Natural insulin includes insulin-derived from the pancreas of pigs and cows. Worldwide, this insulin is currently being phased out and synthetic has been dominating the insulin market.

According to International Diabetes Federation, India currently ranks number one in diabetics between the age group of 20 and 70. The country has a diabetics population of 32.7 million, China 22.6 million, US 15.3 million, Pakistan 8.8 million, Japan 7.1 million, Indonesia 5.7 million, Mexico 4.4 million, Egypt 3.4 million, Brazil 3.3 million and Italy 3.1 million.

IDDT made the following response in a letter to the Editor, The Times of India:

Sir,
I am writing in response to your article 'Synthetic insulin, a safer choice March 7th 2002, which refers to arguments and counter arguments about synthetic insulin or natural insulin for people with diabetes.

Your article and my response demonstrates this point. Dr C.B. Sridhar, professor at St John's Hospital says that unlike synthetic insulin, natural insulin cuts through the blood-brain barrier and causes major side effects including hypoglycaemia. I have to point out that there is evidence that suggests just the opposite and accounts for why a sub-group of people experience loss of warning symptoms with synthetic insulin which return when they change to natural insulins. In addition, after 20 years of being used, there is no evidence from research that shows that synthetic insulin has any clinical benefits for patients over natural.

More importantly, the financial implications of using synthetic insulin with no known benefits, for a country such as India with a high diabetic population, is that synthetic insulin is more than double the cost of natural insulin making it unaffordable for many families. The result is that people are dying for lack of affordable insulin. Our Trust in the UK tries to help by collecting in-date, unopened insulin to send to India and other countries for people who are unable to obtain natural insulin and cannot afford the only alternative - the more expensive synthetic insulin.

We should also understand that natural insulin is being phased out because of the commercial decisions of the pharmaceutical companies, not because there is anything inherently wrong with natural insulin or because people with diabetes have stated a preference for synthetic insulin. Indeed the opposite is true, people with diabetes want both natural and synthetic insulins to remain available to suit all needs, whether these are for health or socio-economic reasons.

Jenny Hirst
Co-Chairman
Insulin Dependent Diabetes Trust- International

The hidden dangers of diabetes

The Independent
3 April 2002.

Barbara Stockham was 45 when she finally received a diagnosis for the health problems that had plagued her for so long. "I was tired night and day," she remembers. "I was always thirsty, was losing weight and constantly needed to go the toilet."

The diagnosis, when it came, occurred almost by accident, as a result of her vitamin B12 deficiency, which required a blood test. It was this test that revealed her abnormal glucose levels, and led to the discovery that Stockham had developed Type 2 diabetes. Her body had stopped producing enough insulin and was gradually becoming resistant to its effects.
Doctors could not tell her when she might have contracted the disease. There was no history of diabetes in her family. "I was devastated when I found out," she says. "I had been to five doctors before I was diagnosed, and no one picked up on the symptoms, even though I had all of them."

At this moment, one million people in Britain have diabetes, and don't know it yet. "The missing million" is a phrase that has become popular currency with doctors who specialise in the treatment of diabetes, and highlights what is being called by some a pandemic for the 21st century, a health emergency comparable to Aids. In the year 2000, it was estimated that one and half million people in the UK suffered from the disease. By 2010, that figure will have increased to three million, by which time it will be costing the NHS one-fifth of its entire budget.
Diabetes is expensive to treat and the vast majority of the money that is spent on the disease goes on treating the complications. The problem is that the symptoms can take up to 12 years to become apparent, by which stage the consequences can be serious.

A year after her diagnosis, Stockham has to inject herself with insulin four times a day. While at least she is treating it, the insidious nature

of diabetes means it had already caused damage, and Stockham is beginning to discover just what that means. “Once you get one immune problem,” she says, “you rarely get away with just one.” As well as the B12 deficiency, which requires an injection every three months, she has developed hypothyroidism - an under-active thyroid, which brings all its own problems. “Diabetes affects your heart, kidneys, circulation, and sight,” she sighs. “Now my 13-year-old son knows how to inject me with insulin, and has to keep a list of telephone numbers in his bedroom to ring if anything goes wrong. It’s a lot of responsibility for him.”

Oddly enough, a large number of sufferers discover their condition in foot clinics. By then, however, damage limitation is often the only treatment left. If diabetes is left too long, it can reduce the blood flow to lower limbs, causing nerve damage to the legs and feet. The numbness that ensues can result in ulcers that the patient cannot feel. If these are allowed to develop, amputation can be the only option.

Dr Kamlesh Khunti, a clinical senior lecturer at the University of Leicester, is adamant that more needs to be done about this situation, but recognises the difficulties. “There is no way that the NHS could cope with giving everybody regular blood tests, but it needs to put out major public-health messages, as well as screening high-risk patients.” By high risk, he means the overweight (more susceptible to Type 2 diabetes), those with a family history of diabetes,
and, surprisingly, those of African, Caribbean or Asian origin.

At the forefront of research on the subject, the University of Leicester has found that the risk of diabetes is two to three times higher in Africans and Caribbeans, and four to six times higher in South Asians. In the London borough of Tower Hamlets, where the ethnic-minority population is high, for instance, doctors are experiencing an epidemic of huge proportions. No specific reasons have been found for this, although Dr Khunti points to cultural factors as a possible explanation. “Already,” he says, “there are genetic risks, but other factors, such as a diet high in carbohydrate and a lack of exercise, could play a large part.”

At the moment, the cause is less important than finding out who has the condition as soon as possible. Without treatment, all major organs are at risk: until 1921, when treatment was found, this was the wasting disease that caused death. The disease hasn’t changed, just the manner of combating it, and so a sense of urgency must remain. Even today, diabetic retinopathy is the leading cause of blindness in adults of a working age in the UK.

The diabetes team from Leicester Royal Infirmary has seized the initiative and started its own screening programme, based in a major shopping centre, targeted at those who are known to be most at risk. Their funding comes not from the health authority but from drugs companies.
If diabetes is caught at an early stage, the consequences do not have to be so drastic. But it is a disease for life. Sam Walker, who is 18 now, was diagnosed five years ago with Type 1 diabetes, the strain that occurs when the pancreas simply stops producing insulin. “It interferes with every part of my life,” Sam says. “Diabetes engulfs you. You have to think about everything you do, even if it’s just going for a walk or eating a meal. I always have to bring food with me if I’m going out for an evening, just in case I get too low in blood sugar.” And if he does get too low, it suddenly becomes difficult to function. “Recently, I had been moving heavy furniture around and had a late lunch. My blood sugar went very low very quickly. It was like a dream. I had money in my hand to buy food but when I was looking at it, I felt as if it was pretend money.” He wandered around on his own for a couple of hours until he managed to make a phone call to his father and asked him to pick him up.

Keith Walker, his dad, is by now used to dealing with diabetes - before Sam, his daughter Chloe was diagnosed at the age of five. “It’s a real body blow when you find out that your child has diabetes,” he remembers. “It’s so traumatic having to put the needle in those tiny legs. But you have to accept it and get on with it.” It’s rare for a family to have more than one child with diabetes, but when Sam started to show the same symptoms, Keith and his wife recognised them instantly. “It’s painful for a family to find out a second time,” Keith says,

“but we found that diabetes is one of those things that can occur to anyone at any time. People need to be made aware of the symptoms so that they can recognise them quickly. The Government needs to do something, but saying that, I don’t know what it can do.”

What doctors want the Government to do is facilitate wider screening services. Yet the Government is refusing to take further action until there is definitive evidence. Its reluctance could stem from the fact that the treatment for diabetes already takes up 10 per cent of the NHS budget, and further measures would be fiercely expensive. In reality, though, it is a case of weighing up the benefits of short-term financial savings against the long-term costs of
allowing one million diabetics to remain untreated. The medical profession is calling it a time bomb, and no one wants to be there when it explodes.

The GM injection

Daily Mail
Jo-Ann Goodwin
August 29, 2002

Tainted crops in our fields. Superweeds that can’t be killed. Fears over mutant cattle, fish and pigs. Recent weeks have brought alarming revelations over GM technology. But does this special Mail dossier reveal the biggest scandal of all?

JONATHON was 19 years old when he died. Tall and strongly built, he was a keen all-round sportsman with a particular passion for football. He had chosen to study law after leaving school, and quickly settled in at Southampton University. On the last night of his life, Jonathon shared a curry with his flatmate, Ben. Exams were looming, and the two students spent a while revising before going to bed. Next morning Jonathon failed to turn up for football practice. His body was discovered later that day. He had died in bed some time in the early hours of April 23, 1995.

To this day, his mother Cheryl is haunted by memories of the police arriving at the door of her Midlands home to break the news. But what haunts her even more is the terrible possibility that Jonathon was killed by the very medication he was taking to keep himself alive.

He had been diagnosed as diabetic just before his 17th birthday. And like almost all sufferers in recent years, he had been prescribed genetically engineered ‘human’ insulin, commonly – and rather misleadingly – referred to as ‘human’ insulin.

Diabetics need insulin to prevent their blood sugar levels spiralling out of control. But in Jonathon’s case, something went catastrophically wrong. The cause of his death was officially recorded as hypoglycaemia – meaning that the level of glucose in his blood had plunged so low that his body effectively ran out of fuel.

‘Hypos’ of varying severity are a constant hazard for diabetics, but in the months before his death Jonathon had suffered them with increasing frequency. They would strike without warning, leaving him disoriented and on the brink of collapse.

His mother now believes that there was a simple and deeply disturbing explanation: Jonathan’s body was unable to cope with genetically engineered insulin. ‘He was put straight on it as soon as he was diagnosed,’ she says. ‘No one told us there was any alternative. It was only afterwards - when it was too late - that I found out that things could be different.’

Indeed, as Jonathon’s mother has discovered, his death is part of a far wider story.

Since its introduction 20 years ago this summer, genetically engineered insulin has been linked not only to an increasing number of unexplained deaths but to a range of side-effects that some patients say have destroyed their lives. These range from unexpected hypos to

massive weight gain, violent mood swings, memory loss, joint pains, mental confusion and crippling exhaustion.

Complaints have been voiced by thousands of diabetics around the world. But they have failed to stop human insulin almost completely replacing insulin derived from pigs and cattle - although the animal insulin doesn't seem to have the same effects. In a striking echo of the MMR controversy, those who dare to question official policy have been vilified as alarmists. Tony Blair, for one, has hailed human insulin as a shining example of the benefits of GM technology.

Now, according to campaigners against human insulin, the need to challenge such complacency has never been greater. They fear that recent developments in the pharmaceutical industry could soon choke off all remaining supplies of alternative medication. They speak of feeling 'the noose tightening around our necks', and warn that more tragedies like Jonathon's are inevitable unless urgent action is taken. Now their campaign has received a major boost with the publication of a damning report on research into the new insulin. It challenges the reliability of trials that supposedly gave the product a clean bill of health.

Concerns over GM technology tend to concentrate on th4 crops in our fields and food on our plates. But insulin is a substance that thousands of diabetics inject directly into their bodies every day. For the drug companies involved, millions of pounds in profits are at stake. And as the unsettling saga shows, profits can sometimes seem to be more important that the interests of patients.

At the beginning of the 1980s, two corporate giants were engaged in a breakneck race. Eli Lilley and Novo - later to become Novo Nordisk – were vying for control of the lucrative worldwide insulin market. Previously, all diabetics had relied on animal insulin extracted from the pancreases of pigs and cattle. But the bright new dawn of bio-technology had arrived, and Eli Lilly had succeeded in cloning a synthetic form of the insulin molecules found in the human body.
It was an astonishing breakthrough - but Novo already held 40 per cent of the UK insulin market and had no intention of losing it to Eli Lilly. Concentrating resources, it quickly caught up with its rival.

By 1981, Novo had its own genetically modified product. Although described as 'human' insulin – a public relations masterstroke, that helped ensure its acceptance by diabetics – it was, in fact, synthetic. Today it is manufactured from yeast cells or E coli bacteria.

The insulin was put before the Medicines Control Agency, a government body which checks the safety of drugs before licensing them for sale. Novo was desperate to get its product on the market before Lilly's, and found the MCA officials extremely co-operative.
'It was cutting-edge science and very glamorous,' says Dr Laurence Gerlis, who was then Novo's director of medical research but is now an outspoken critic. 'The MCA were keen to be seen encouraging bio-technology.'

Opponents of human insulin now suggest that the MCA failed to demand sufficiently rigorous clinical trials for what was the first genetically produced drug to be licensed in Britain.

The first research using human insulin had been carried out in 1980 using just 17 people - none of them diabetic, and all of them men - and it seems that the pre-licensing trials were carried out on a group of only 300. Nowadays, trials generally involve groups of 1,000 to 1,500. But back in the 1980s, according to Dr Gerlis, standards were not so demanding. 'We just had to prove that this really was insulin,' he says.

To market the new drug, Novo's intention was to employ a 'substitution strategy'. If the company could persuade its existing animal-insulin users to switch over to the human version, it could effectively clean up before Eli Lilly's launch in September 1982. The medical justification for this strategy depended on the new product having an identical effect on the human body to insulin from pigs. But when Novo's medical

advisory committee met in Copenhagen in April 1982, Dr Gerlis told the marketing men the bad news: animal and human insulin were not the same.

Pork insulin is less soluble than human insulin and has different amino acids. Crucially, says Dr Gerlis, human insulin is faster and more aggressive in its effect on blood sugar levels. As far as Dr Gerlis was concerned: 'We were asking for a licence to market human insulin, not for permission to entirely replace the existing pork insulin. There is an important difference.' He and his committee advised that the substitution plan should be abandoned.

At the launch two months later, however, Novo announced that 'human insulin supersedes porcine insulin'. The company signalled its intention of gradually withdrawing pork insulin from the market.

The marketing men had over-ruled the medics - and the vast majority of British diabetics subsequently followed their consultants' advice and switched to the new product. Some were simply handed the new insulin when they presented their prescription at the pharmacy, without realising anything had changed.

Most patients appeared to adapt without problems and it should be stressed that this continues to be the case. But by the mid to late Eighties, reports began to surface suggesting that a sizeable minority were suffering difficulties. They spoke of finding themselves 'operating on automatic pilot', feeling confused, tired and ill, or undergoing such severe personality changes that relatives felt they were 'no longer the same person'.

Then there were the mysterious deaths. Often the victim was young – in their teens or twenties - and living alone. They went to bed in apparently perfect health and never woke up. It was dubbed 'adult cot death' or 'dead in bed syndrome'. Such sudden tragedies had happened before among diabetics, but usually there was evidence of convulsions prior to death. With these cases the bed was entirely undisturbed. The victim had died without trauma or struggle and without apparent cause.

The stories are heartbreaking. In April of this year, 15-year-old Selina Trapp from Derby spent the evening at a friend's house and was home promptly for 9.30pm, just as she'd promised her parents. She had supper, chatted with her mother, watched a little TV and went up to bed. She was a healthy, lively girl, whose diabetes didn't prevent her enjoying a full and active life.

She was found by her mother at just before 7 o'clock the following morning.

She was lying face down on the bed, and wouldn't respond to efforts to wake her. Her father gave the kiss of life but it was too late. The verdict at the inquest was 'death due to hypoglycaemia'.

One of the youngest victims was eight-year-old Zoe Burbridge from Northampton, who died in her sleep in 1994. Her mother, Deborah, is convinced that human insulin was to blame.

It seems that in a significant minority of patients - perhaps around five per cent - human insulin blocks the body's warning signals when blood sugar levels become dangerously low. Such undetected hypos can swiftly lead to coma and death.

In normal circumstances, the diabetic is alerted to the onset of hypos (even when asleep) by sweating, shaking and feelings of faintness. These worrying signals allow the diabetic to swallow a chocolate bar or fizzy drink, replenishing their blood sugar so that all is well again. But mounting evidence suggests that in some cases genetically engineered insulin entirely masks the onset of hypos, allowing the patient to slip into coma without warning. Increased frequency of hypos may also cause damage to the nerves that control the heart.

By the late 1980s more than 80 per cent of British diabetics were injecting human insulin and concerns were increasing. In the space of two years, the British Diabetic Association received more than

3,000 letters of complaint. In 1990, it announced it was setting up a research project directed by Dr Natasha Posner to investigate. Dr Posner submitted her report the following year, but the BDA – which receives roughly one third of its annual income from pharmaceutical companies - announced that it would not be publishing the findings as they were felt to be 'too alarmist'.

Substantive evidence about the safety of human insulin remains hard to come by. One Liverpool University study reported in the Lancet, which found no difference between human and animal insulin, studied just seven patients. As Jenny Hirst of the Insulin Dependent Diabetes Trust, a patients' pressure group, points out: 'If adverse reactions occur in around five per cent of diabetic users, how do you judge five per cent of seven patients?'

Dr Laurence Gerlis, the former Novo Nordisk research director, is equally sceptical about tests purporting to give human insulin a clean bill of health. 'It is very difficult to prove a negative in clinical trials,' he says. 'The same problem comes up with the MMR vaccine. How do you prove MMR doesn't cause autism? The trouble is that the effect may be there, but your tests have failed to show it.'

This cuts both ways. In the absence of research studies, defenders of human insulin feel able to dismiss stories of harmful side-effects as mere 'anecdotal evidence'. But as Dr Gerlis explains, there is a long history of such anecdotal reports being accepted as grounds for concern. It's simply a matter of listening to the people who actually use the drug in question.

'If a drug appears to be showing adverse effects, then we take it off the market. Eli Lilly's Opren drug for arthritis is an example. But in this case we have failed to listen to what patients have told us.'
By 1991disillusionment had set in and 400 UK diabetics joined together to take legal action against Novo Nordisk. More than 30 lawyers were involved, and strategy committees were set up in England and Scotland. Solicitor George Hann sat on the Scottish committee and was charged with responsibility for securing expert medical witnesses to support the case against human insulin. A respected legal figure and himself a diabetic, he remains astonished by what happened next.

Mr Hann wrote to over 20 diabetologists asking if they would be prepared to help. He got only one response, which was negative. Otherwise there were no replies. When he investigated, he says, he discovered that all the consultants were now receiving research grants or consultancy fees from Novo Nordisk. Although there is no suggestion of impropriety, this clearly torpedoed any chance of them giving evidence for the dissident patients. 'Novo Nordisk were very quick off the mark,' says Mr Hann. 'They had bought up every diabetologist in Scotland. Without medical opinion we couldn't take it any further. The action was effectively stymied.'

Another Edinburgh solicitor confirms this extraordinary story. 'As I recall,' he says, 'every single diabetic specialist seemed to be a paid official consultant to Novo Nordisk. That created a potential conflict of interest that prevented them from being used as witnesses. It very effectively pulled the rug from under us.'

Novo Nordisk denies any attempt to silence the consultants, but it was sufficiently troubled by the threat of litigation to have appointed a PR firm, Key communications, with a brief to 'defend the safety profile of genetically engineered human insulin'.

When the English legal action collapsed, because patients were unable to obtain legal aid, Key Communications was triumphant, 'Novo's reputation remained intact among patients, health professionals and media' the company boasted.

The rebel patients remain unconvinced. Much of the case centred on so-called 'double blind' trials - in which neither the doctors nor the patients know which type of insulin is being administered. But some diabetics who had already reacted badly to genetically engineered insulin had refused to take part, because they were so scared of its effects.

Critics also point out that one of the crucial trials, conducted at King's Hospital in London, involved just 17 patients and gave them only two months to see if they reacted badly to the new insulin [[other evidence suggests adverse symptoms may appear only after a year or more]. The trial was directly funded by Novo Nordisk. The company's medical director, Dr Alan McDougall, insists that the work was totally independent. 'It doesn't mean in any way that research is biased because we funded it,' he says.

Novo's promotion of human insulin has also been aggressively supported by the British Diabetic Association.

In 1996 Lawrence Gerlis and Dr Matthew Kiln - a GP and critic of human insulin - each received a letter from Professor Harry Keen of the BDA in which he accused them of 'professional misconduct' because their critical stance would frighten the majority of diabetics happy with human insulin. Dr Gerlis says both he and Dr Kiln were put under 'tremendous pressure, especially by the BDA'. In 1997, the BDA placed a number of
advertisements in Sunday newspapers to denounce Dr Kiln as 'irresponsible'. 'Why,' asks Dr Gerlis, 'should a charity that raises money from patients take such a role?'

The charity, now renamed Diabetes UK, is unrepentant. It agrees that there 'was a concern' about the safety of human insulin, but insists 'there is no evidence to back it up'.
Now, however, a report from the Cochrane Collaboration – a respected organisation that reviews medical research – has attacked the 'poor methodology quality' of most of the trials. The report found that 'patient-orientated outcomes' – meaning quality of life to death rates were not investigated with sufficient rigour. It also found no proof that the new insulin was superior to its animal-based predecessors.

Concerns about the new isulin are not confined to the UK, however. Canada has recorded 121 instances of human insulin causing seizures, convulsions and extreme hypos, whilst the American Food and Drug Administration says it has received 'thousands' of similar reports.

'There are individual cases you can't explain,' concedes Dr McDougall of Novo Nordisk. 'No one knows why these young people are dying.'

As well as Novo Nordisk, which has by far the largest market share, genetically engineered insulin is now supplied in the UK by Eli Lilly and a third company, Aventis
Pharmaceuticals.

For the critics, the central issue is choice. Many doctors fail to inform patients that alternatives to human insulin are available, or that some diabetics seem to react badly to it. New patients are invariably put straight onto human insulin without explanation. Yet many of those who experience unpleasant side-effects report almost miraculous improvements once they switch back to pork or beef.

Shirley Stone, 59, from Hertfordshire, spent eight years suffering from 'horrendous symptoms' - palpitations, painful joints, aggression and constant fungal infections - after being switched to human insulin without consultation. The symptoms stopped 'overnight' when she returned to animal insulin.

Beverly Freeman, 31, from Northampton, underwent a similar transformation.

After being put on human insulin at the age of 12, her weight ballooned to15 stone and she suffered from constant exhaustion. 'It was like having really bad PMT three weeks a month,' she says. 'In effect, I lost my teenage years. I was so unwell that I was forced to drop out of school and my education was totally disrupted.' Switching to animal insulin at the age of 23 changed her life. 'I felt better within four weeks,' she says. She now has a degree, a family, and a job campaigning for the Insulin Dependent Diabetes Trust.

But Beverly and Shirley, like many others, are haunted by the fear of having to return to genetically engineered insulin of alternative

supplies are not maintained. Although Novo Nordisk still produces a limited amount of animal insulin, the company intends to discontinue it over the next few years. The company insists it would not leave people ‘high and dry’, adding that ‘if we withdraw animal insulin in the UK we would give a minimum 18 months’ notice’. But this does little to reassure people like Beverly and Shirley.

Animal insulin is no longer on offer from Novo Nordisk in France, Germany, Belgium, Holland, Canada and Australia. Although it remains available in Britain through a small independent company, CP Pharmaceuticals, there are many who fear for the future.

These fears have risen since last December, when Novo Nordisk bought up a
Brazilian company called Biobras which is the world’s main supplier of the raw materials needed to make animal insulin. Two months ago, Novo chairman Viggo Birch wrote to assure Jenny Hirst, of the Insulin Dependent Diabetes Trust, that ‘in the short term’ the company had no plans to terminate the production of animal insulin at Biobras. Developments in the ‘long term’, however, would ‘be in line with our strategy to discontinue production of unmodified animal insulin’.

‘There are a lot of people living in fear of animal insulin being withdrawn,’ says Shirley Stone. ‘If it is, they’re going to be in terrible trouble.’

Once again, it seems, the voice of the patient is going unheard.

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