# Insulin Dependent Diabetes Trust

October 2000 Newsletter

Registered Charity No 1058284 - Issue No 26


## The Past Has A Way Of Coming To Haunt You!

This is not a new expression by any means but often very apt. The internet has a way of enabling the past to re-emerge because we can search for information and our searches can lead in all sorts of odd directions! People who live in countries where animal insulins are no longer available are desperately searching for information that may help them. One such person in the States turned up a fascinating piece of history from the UK that was news to us, but confirmed some suspicions!

**Key Comminications**

This is a public relations company advertising their expertise on a web site [ref 1] saying that organisations use communication as a process in the achievement of their corporate objectives in various areas such as media relations, culture change and crisis management. In other words, PR companies are employed to present a message or image, to try to change a belief and/or to counteract any adverse publicity. The advertisement cites their achievements for various different companies. One of the companies listed is Novo Nordisk and Key describe the work they undertook for them in the early 1990s when there was an attempted class action in the UK against Novo. It makes interesting reading and here is how they report their work for Novo Nordisk:

**Brief**

- Defend the safety profile of genetically engineered human insulin

**Solution**

- A counter communication campaign was needed.
- A reactive strategy was recommended despite 'internal client pressure to actively promote human insulin'. When approached by the media we were open and helpful.
- The issues/crisis management programme spanned three years. We deliberately avoided direct media confrontation with patients and representatives of patient groups.
- Headquarters and UK medical spokespeople were media trained.
- Extensive, rapid media monitoring of diabetes stories world wide enabled identification of claim conscious lawyers and preparation of reactive press statements.

**Results**

- Legal action collapsed [two key double blind trials found in favour of human insulin]
- Following the trial results, legal aid was denied and litigation collapsed
- Novo's reputation remained in tact among patients, health professionals and media
- Sales of human insulin continue to grow
- Medical professionals accepted that human insulin has an excellent safety profile.
- The specific use of insulin from genetically engineered sources never developed as an issue.

I am sure we could all disabuse Key of some of these conclusions! Many of our members were either part of this class action or watched on the sidelines with a very personal interest, as I did. At that time we were all rather naïve and had no idea that a PR company was manipulating the situation. Nor did we know that there was a deliberate policy that Novo Nordisk were not to be publicly answerable, let alone that the doctors appearing in the media to defend human insulin had been media trained at the expense of the company that made it! This is yet another example of the cosy relationship between members of the medical profession and industry that cannot be in the best interests of patients.

The results claimed by Key Communications may well not be entirely true, it is after all an advertisement selling themselves, but it leaves a nasty taste. Was the judgement that 'human' insulin had an excellent safety record really based on the results of two trials? Did the legal action really hang on the results of only two trials and if so, were those trials deliberately carried out during this three-year period for this specific purpose, who instigated them and who funded them?

Perhaps worst of all is the realisation that a PR company had to be employed to defend the safety of a drug. If the safety of 'human' insulin could not be defended on the basis of scientific evidence, then the randomised large-scale, long-term trials to evaluate its safety and adverse reactions should have been insisted upon by the doctors/researchers/experts in diabetes.

Ref 1 www.keycommunications.co.uk/solutions/novonordisk.htm

## Lord Hunt Responds... After 10 Weeks!

In the last Newsletter we provided readers with the information from a press release from Aventis, one of the world's three largest insulin manufacturers. Prior to doing this we twice contacted Aventis, who did not respond, the Secretary of State for Health, the Medicines Control Agency [MCA] and the Committee on Safety of Medicines [CSM]. We told them of our commitment to people with diabetes to keep them and all those with an interest in diabetes fully informed. We asked them to take action before July 1st. IDDT received no response whatsoever 7 weeks later and had to assume that again our pleas had fallen on stony ground. We therefore went ahead with our plans to pass on the information supplied by Aventis. [A reply was eventually received some 10 weeks after our original letter was sent.]

Just to remind you, here is the statement from the Aventis

press release:

"Safety Information:

Human insulin therapy may be associated with hypoglycaemia, worsening of diabetic retinopathy, lipodystrophy, skin reactions (such as injection-site reaction, pruritus, and rash), allergic reactions, sodium retention and oedema."

**Don't shoot the messenger!**
We did receive a few critical and even unpleasant letters from doctors and health professionals but not one letter from an actual patient complaining that we were being alarmist and there were several who expressed their gratitude.

The answer is simple: 'Don't shoot the messenger'. IDDT did not put it in the public domain, we merely passed on information in a press release from a reputable pharmaceutical company who clearly intended that the information should reach the public – the purpose of a press release!

- To the accusation that we have been 'disingenuous' – the exact definition 'not sincere, lacking in candour'. Need I defend this accusation? I am usually accused of being too forthright, certainly not lacking in candour! Not sincere – dear me! Why does anyone imagine that we are doing this for any other reasons thaN absolute sincerity? Where is the gain? When it comes to being disingenuous, I think perhaps the expression is better used on those that have failed to listen to people with diabetes over the last 15 years and those who have chosen to ignore the fact that the evaluation of 'human' insulin was inadequate.
- To those who say that we were being threatening by suggesting that prescribers should note the warning statement made by the Medical Defence Union in Pulse, May 20th – again IDDT merely acted as a messenger, the warning was not made by us.
- To the anonymous Healthcare professional from Carmenthenshire NHS Trust who says that our Newsletters have no credibility – we cannot cross you off the mailing list unless you declare yourself!
- To the doctors that say that the information is already well-known – it may be well known to them but it certainly wasn't, and isn't, well known to patients.
- To those that deny that 'human' insulin causes worsening of retinopathy - some professionals saying that these side effects are well known and some denying they exist! Where does this leave patients? Which group is right? Where is the evidence from long-term studies to compare the effects of treatment with animal insulin and 'human' insulin on the development of retinopathy?

It does not require a rocket scientist to see why 'human' insulin may cause worsening of retinopathy:

1. 'Human' insulin can cause loss of warnings in some people – this is in the data sheets and Patient Information Leaflets for 'human' insulin.
2. Loss of warnings leads to a greater risk of more frequent and/or more severe hypoglycaemia.
3. When hypoglycaemia is severe and reaches the point of neuroglycopenia [the brain starved of glucose] it has specific deleterious affects on the central nervous system. The retina is vulnerable to hypoglycaemia because it has an unusually active metabolism. [Ref 1,2] This has been known for decades.

**Conclusion**
People that do suffer more hypos with 'human' insulin are at risk of worsening of retinopathy caused by hypoglycaemia affecting the metabolism of the retina. If their hypos are reduced or less severe with a change to beef or pork insulin, then their chances of worsening of retinopathy from this cause may be reduced. Indeed, hypoglycaemia causes all the adverse reactions listed by Aventis, regardless of the type of insulin used. So while 'human' insulin per se, may not be directly responsible for them, the increased hypoglycaemia that 'human' insulin causes in some people may well be.

It must follow that when prescribing 'human' insulin consideration

should be given to other known risk factors for retinopathy that may put some people at greater risk when using 'human' insulin. Some of these risk factors are known:

Long duration of diabetes - twenty years after diagnosis almost all those with Type 1 diabetes and 60% of those with Type 2 diabetes will have some degree of retinopathy.[ref 3]

Pregnant women are susceptible to retinopathy developing during pregnancy.

Children and adolescents in the long term are at greater risk of microvascular and macrovascular complications of diabetes. This paper recommends that surveillance for the earliest evidence of microvascular disease should begin at puberty and after 3 and 5 years of diabetes. [ref 4]

**Lord Hunt's reply**

In the interests of presenting all views so that people with diabetes are able to make informed choices about the type of insulin they wish to use, here is Lord Hunt's reply:

"Your letter refers to concerns regarding hypoglycaemic unawareness with human insulin. A considerable number of scientific studies have been performed comparing human and animal insulin. The Committee on Safety of Medicines has considered the available evidence on a number of occasions and has concluded that, although some patients have experienced problems on transferring from animal to human insulin, and that some patients may be better suited to animal insulin, there is no evidence of a specific safety problem with human insulin which is well tolerated by most patients.

I am concerned that the statement you quote from Aventis may have been taken out of context. All injected insulins, both human and animal, may cause hypoglycaemia, lipodystrophy, skin reactions and allergic reactions. These are not specific to human insulin. Furthermore oedema is a common complication of long standing diabetes. Intensive glycaemic control has been shown to lead to short term deterioration in retinopathy but long term there is an improvement in eye disease.

It is of paramount importance that if new evidence emerges relating to the safety of any treatment including insulin, that this is investigated and critically assessed. The Medicines Control Agency and CSM are responsible for the continuous monitoring of the safety of all licensed medicines and the safety of insulin is therefore under continuous review. Monitoring the safety of medicines includes assessments of reports of suspected adverse drug reactions from the UK, via the Yellow Card Scheme and from abroad, continuous scrutiny of the medical and scientific literature and review of the safety reports produced by manufacturers. I would be grateful if you could provide the MCA with a copy of the statement from Aventis and any other evidence you hold relating specifically to these suspected reactions. The MCA would be particularly interested in any data suggesting that there are specific problems with human insulin and will be contacting the marketing authorisation holders.

I share your concern that people with diabetes should have the best possible information about risks and benefits of their treatment. For this reason I would ask that you refrain from dissemination of information which may cause unnecessary alarm or confusion, until the MCA has had an opportunity to properly evaluate any new evidence available."

In replying to Lord Hunt we remembered that we mustn't shoot the messenger either. He is a messenger too but for the MCA's experts in diabetes so our response included the following comments:

- We consider that we have acted with responsibility by contacting Aventis twice for information and contacting the Department of Health before we informed people with an interest in diabetes.
- We believe in openness and have a commitment to keep people with diabetes informed. Failure to inform our members means withholding information from our client group, people who live with diabetes, and information is the key element to being able to make an informed choice of insulin treatment, in line with the

Patients' Charter.

- The MCA's stance might be more supportable if they advised that when ' human' insulin, consideration should be given to other known risk factors for retinopathy that may put some people at greater risk when using 'human' insulin.
- The MCA continues to look only at the safety of human insulin per se. While having to accept hypoglycaemia as an adverse reaction to 'human' insulin, the MCA fails to recognise the consequences of hypoglycaemia and the complications it may cause.

Ref 1 Kalimo H, Olssen Y: Effects of severe hypoglycaemia on the human brain-neuropathological case reports. Acta Neuro Scand 1980; 62:345.

Ref 2 Vital CI, Picard J, Arne L, et al: Pathological study of three cases of hypoglycaemic encephalopathy. Le Diabete 1967; 12F:291-296

Ref 3 Klein R, Klein BE, Moss SE, et al. The Wisconsin epidemiologic study of retinopathy. III. Arch Ophthalmol 1984; 102:527-32

Ref 4 Endocrin Metab Clin North Am 1999 Dec;28[4]: 865-82

## NovoPen 3 Adverts - IDDT Makes Formal complaint

Soon after pens became available on the NHS, one of our members, Mr Smith, received an unsolicited letter and leaflet about the NovoPen 3. The letter was on headed Novo Nordisk paper and signed by a member of their staff and headed "Information for people with diabetes." It included the offer of a free video that demonstrates the device and includes interviews with patients and specialist nurses. Mr Smith was angry because he did not know how Novo Nordisk had received his name and address and because NovoPen 3 can only be used with 'human' insulin – a treatment he has had to regularly fight against with his clinic. On behalf of Mr Smith, IDDT made an official complaint to the Association of British Pharmaceutical Industries [ABPI] on the following grounds:

1. Confidentiality –how did Novo Nordisk know his name and address and how did they know he had diabetes, especially as he did not use the insulin for which the pen was suitable?
2. Promotion of medicines –pharmaceutical companies are allowed to advertise medical devices to patients but they are not allowed to advertise medicines. However, the NovoPen 3, unlike earlier pens, has been designed so that it can only be used with Novo Nordisk 'human' insulins. It therefore appeared that this advertising package was indirectly advertising a specific brand and species of insulin to him.

IDDT argued that the very nature of the advertising material he received from Novo Nordisk was trying to persuade him to use its pen and therefore its 'human' insulin and that this was a breach of the regulations forbidding advertising medicines directly to patients. If it was not an actual breach it could be interpreted as circumventing the regulations to persuade him to ask his doctor to prescribe this particular pen and therefore this particular insulin.

Results:

Confidentiality – this complaint was not upheld. Novo's explanation was that after Lord Hunt's announcement that pens would be free on the NHS, they sent a mailing to 15,000 randomly selected households that had indicated in a consumer products survey that someone in the house had diabetes. The names and addresses were not known to Novo Nordisk.

Promotion of medicines – this complaint was upheld on the grounds that the mailing and video constituted an advertisement of a prescription only medicine and that they would both encourage patients to ask their doctors to prescribe NovoPen 3 and in effect a Novo Nordisk insulin cartridge.

Both sides have the right to appeal against the decisions. IDDT did not appeal on the confidentiality issue. We might think that a mailing to 15,000 households that just might have someone that requires insulin treatment as opposed to the much more common tablet treatment, is an excessive expenditure but that is not the issue. The Appeal Board did express concern about the original letter being misleading and they advised that it should have explained that it had been sent by a third party.

Novo Nordisk did appeal against the decisions on promotion but their appeals were unsuccessful and they have given an undertaking to discontinue the mailing and to avoid a similar breach of the Code in future.

## Islet Transplantation And More - JDF help with funding

THE JUVENILE DIABETES FOUNDATION [JDF] was founded in America with the very focussed aim of finding a cure for diabetes. They have raised huge amounts of money for research and annually they have a 'Walk to Cure Diabetes' which this year aims to raise £42 million in 5 countries! The JDF have had an operation in the UK for some years now. Modern technology makes the possibility of a cure seem more realistic. Here are details of just two projects funded by the JDF:

Islet transplantation – the successful transplantation of insulin producing islet cells in 8 people with very difficult to control Type 1 diabetes in Canada is being followed up by further trials. These will involve 40 people aged between 18 and 65 who are unable to control their blood glucose levels despite rigid insulin regimes. The trials will initially take place in Canada and the US and then in Switzerland, Germany and Italy. In the US the National Institutes for Health [NIH] and the Juvenile Diabetes Foundation [JDF] will each provide 5 million dollars to 10 centres.

According to statements from the head of the research team, James Shapiro, their method of transplantation succeeded, for the following reasons:

- They tried a new combination of anti-rejection drugs that did not include steroids.
- They modified the way islets are harvested from a pancreas, eliminating the uses of substances containing non-human proteins that might trigger rejection.
- Only freshly isolated islets were transplanted rather than frozen or cultured ones.

The actual transplantation is relatively simple as the islets are injected into a blood vessel in the liver with the patient needing only a sedative and local anaesthetic and able to go home the next day. One obvious problem for the future is the shortage of donor pancreases as islets cannot be obtained from living donors. [Only about 5,800 people in the US and 600 people in Canada donated organs after death last year.]

Identifying and isolating pancreas stem cells – this involves finding out how beta cells develop normally during the human embryonic life and knowing when beta cells first mature from their precursor cells, which genes regulate the process and when they act. The researchers then aim to duplicate the process outside the human body and to see how well the cells mimic the function of the normal adult beta cells in producing insulin in the same way and in response to the same stimuli. If they are successful then this could provide a future source of insulin producing cells for transplantation.

Single injections of raw DNA – scientists have found that pieces of insulin gene when injected into laboratory animals, will trigger the production insulin. Until recently it was assumed that if DNA was injected into the blood stream without a protective coating, it would be broken up by the body's immune system. However, scientists have

found that patients with cystic fibrosis and muscular dystrophy will respond to direct DNA injections. Now scientists in Aberdeen have found that unadulterated DNA can produce a similar effect on insulin production. They took the gene that makes insulin and spliced it into the muscle cells in rats. They were then injected back into the animal's leg muscles and they began to make insulin that could be released into their blood stream. This is a long way off being able to be used in humans and would require surgery two or three times a year. But the researchers also took the insulin gene of humans and grew millions of copies of it and then injected these directly into rats. It was then found that human insulin was being secreted into the animals' blood. If this could be developed, it would mean that surgery could be avoided.

More information from the JDF at their web site www.jdf.org.uk

## "Profits Obscene" says US Senator - Awsome 1999 Performance By Lilly

1999 figures for the 12 top pharmaceutical companies show insulin manufacturer Eli Lilly top of the list with a profit return on equity of 54%. As a percentage of sales they spend 21.0% on cost of goods, 27.6% on marketing and 17.8% on research and development.

Interesting that Lilly only spends 17.8% of their total sales on research and development [R&D] but 27.6% on marketing! The pharmaceutical companies nearly always defend their profits by saying that they are different from other industries because they have such a high commitment to R&D. It seems that they have a far greater commitment to selling! I can't resist pointing out that with a profit like this, one would have thought that Lilly could think of the people who are providing their profits and continue to produce animal insulins in the US, even if this is to a diminishing market! No wonder they need to spend nearly a third of their sales on marketing!

NB. We cannot give similar figures for Novo Nordisk because we have no access to this sort of information.

. A further report says that the global pharmaceutical market grew by10% in 1999, up from the 6% growth of 1998, with $207 billion in sales, $90.8 billion of this was in the US and $53.9 billion in the major European countries.

Fortune 500 listings shows that Merck & Co Inc. is the richest drug company with $10 billion in total profits, more than the total profits for the 24 companies in the motor vehicle and parts industry in the US including General Motors in Detroit and Ford in Michigan. In the US pharmaceutical company profits are a political issue because many people cannot afford the high prices that are charged. At a press conference Senator Paul Wellstone said "We have an industry that makes exorbitant profits off sickness, misery and illness of people and that is obscene."

I doubt that anyone with any sort of conscience could disagree with this statement.

## Avandia - The New Drug For type 2 Diabetes

In August the National Institute for Clinical Excellence [NICE] approved the new drug Avandia [rosiglitazone] for the treatment of Type 2 diabetes in some patients. It hit headlines because it is has the potential to be the most expensive drug that NICE has yet approved, costing £320 to £640 per patient per year. NICE estimate that it could be used in 72,800 people and that its use in place of insulin could cost an additional £14.5 million per year in England and Wales. This approval means that there should be no 'post code' prescribing of Avandia.

It is good that Newspaper reports only say at this stage that Avandia

is believed to give better protection against damage to blood vessels and may also delay or prevent some people with Type 2 having to go on to insulin. Just as it should be, no promises without evidence gained from use over time.

Avandia belongs to the family of drugs called thiazolidinediones which includes

troglitazone [Rezulin in the US], withdrawn from the market in the UK only 6 weeks after it's approval because it was shown to cause liver failure. The FDA in the US admitted that Rezulin had been responsible for around 90 deaths from liver failure before they withdrew it more than two years after the first death and after 'whistle-blowing' by some FDA advisers. Like troglitazone, Avandia was also granted fast track approval by the FDA but it was found to be far less toxic than its predecessor. Nevertheless, the troglitazone story was not a happy one and one that is not unfamiliar - fast approval, patients not being fully informed, side effects being ignored and the potential for a great deal of money to be made by industry. SmithKlein Beecham increased their half-year profits by 14%, generating £114 million in the first quarter, largely as a result of what business analysts describe as 'Avandia's outstanding performance' with doctors in the US having written more than 3 million prescriptions in the first year.

Understandably there may be concerns about Avandia so we are providing information from US medical journal adverts and the UK Pharmaceutical Journal, August 26, 2000.

About Avandia

- It is a tablet that works by helping the body to make better use of its own insulin whereas the other tablets for Type 2 stimulate the pancreas to produce insulin. The pre-licensing clinical trials were carried out in 4600 people with 3300 of them using it for 6 months or longer and 2000 for over 12 months.
- Avandia is for use in Type 2 diabetes. NICE recommends that it is only used in people where blood glucose levels cannot be controlled with combinations of the traditional drugs, metformin and/or sulponylurea. It can be used on its own or in combination with a sulphonylurea or metformin. NICE say it should be added to the other tablets rather than substituted for them and that there is no direct evidence from comparative trials that adding Avandia to metformin or to sulphonylurea is any more or less effective at improving control than moving to a metformin plus sulphonylurea combination.
- As it is only active in the presence of insulin, it should not be used for Type 1 diabetes.
- Used in combination with the other tablets it may cause hypoglycaemia.

NICE says that Avandia should not be used in patients with heart failure, liver failure or severe renal insufficiency.

The adverts for Avandia in the US say:

- It may, like other drugs in its class, cause ovulation in some pre-menopausal women and they may be at increased risk of pregnancy so adequate contraception should be advised. This possibility has not been investigated in specific clinical trials but is listed as a precaution by the manufacturers.
- Avandia should be used with caution for patients with oedema, as mild to moderate oedema was reported in the trials. Fluid retention was reported and so people at risk of heart failure should be monitored - check with your doctor.
- Although clinical data show no evidence that Avandia can cause liver problems, because it is the same family of drugs as troglitazone, it is recommended that patients using Avandia have periodic liver enzyme tests until further information is available.
- The most common adverse reactions in the trials with Avandia were upper respiratory tract infection, injury, headache and back pain.

Just a comment - the continued debate in the medical press about whether prescription drugs should be advertised direct to the public in

the UK seems a bit futile. All the manufacturers have to do is issue a press release about their new wonder drug and it is taken up in force by the newspapers, with little or no control over what they say.

## Volunteers Needed In West Wales

Whitland Research Laboratories are continuing their efforts to produce a non-invasive method of blood glucose testing – hopefully so finger pricks will be unnecessary in the future. They do need volunteers again just to provide a few finger prick blood samples to compare these results with their new technique. Members of IDDT have helped before and anyone willing to volunteer and living near Whitland should contact: Yvette Brown at Whitland Laboratories Ltd, Whitland Abbey, Whitland or e-mail y.brown@newscientist.net

## Medicines control Agency And Experts Come Under Fire!

The Medicines Control Agency [MCA] is the UK body concerned with all matters related to drugs and now homeopathic remedies. The Committee on Safety of Drugs [CSM] is part of this body that monitors the safety and efficacy of drugs and collects adverse reaction reports. The committees of the MCA consist of doctors and academics who are experts in their fields and their advice is crucial in deciding whether a drug should be licensed or withdrawn from the market but much of their work is shrouded in secrecy. It is understandable that there is a need to protect the commercial confidentiality, but this body was set up for our protection after the thalidomide tragedy and it would seem that the best way to reassure the public is to make their information accessible to us. IDDT members lobbied their MPs when the Freedom of Information Bill was discussed, 'open government' was introduced but little appears to have changed at the MCA. But we are not on our own in our concerns!

CSM ATTACKED OVER DELAY IN SECRECY – the BMJ 15 July 2000. Ten months ago the Health Service Ombudsman upheld complaints of undue secrecy about the operations of the CSM who then promised to publish edited minutes of their meetings on the internet. Social Audit, a pressure group that monitors the pharmaceutical industry, were told by the MCA, 'Summaries will be published from March 1998 onwards and will disclose details of interests and products where appropriate regulatory action has been completed.' But this promise has still not been fulfilled with only four meetings in early 1998 being published on their web site [www.open.gov.uk/mca/csmhome.htm].

The Dept of Health say preparing the summaries is very intensive work and they have not been able to allocate the resources to it. Social Audit believes the delay is due to the committee deciding to rewrite the minutes for publication in order to protect confidentiality. In the US, the FDA just puts a black line through the parts that need to remain confidential – sensible and speedy!

SCANDAL OF DRUG DOCTORS' SHARES - the Sunday Express, August 6, 2000 exposed the information that more than 170 of the MCA's 248 advisers, doctors and academics, have financial links with pharmaceutical companies and a total of 42 own shares in a variety of these companies. The size of the holdings has been kept confidential until now because the members are not required to disclose on the MCA's register of interest just how many shares they own. The Express information is based on the drug companies' own share registers. More than two thirds of the doctors and academics advising the MCA have investments or receive drug company cash for consultancies, conferences abroad and research grants

The extent of the links between the experts and industry leaves the committees open to allegations of conflicts of interest and that doctors may have an unfair advantage in share-dealing because they are privy to confidential, price-sensitive information. Nicholas Harvey, the

Liberal Democrats' health spokesman, has called for a tightening up of the regulations governing the advisers' interests: "If these experts still have large personal pecuniary interests in the drug companies, we cannot be confident they are making objective decisions." Health Minister, Lord Hunt said on radio that he was satisfied that the experts "do declare an interest when it is required". What he hasn't done is to say who decides when it is required!

The MCA has the power to give or revoke a drug's licence and medicines which have taken years of expensive research to produce can be banned or withdrawn from sale if the committees consider there is cause for concern. The pharmaceutical companies know this only too well and Tom Moore, a former senior executive for AstraZeneca, told the Sunday Express that the drug companies go out of their way to build strong links, saying: "Their objective is to get as close as possible. They are an extremely powerful lobby group because they have unlimited resources."

## Relationship Between Doctors And Industry Too Cosy!

ACADEMIA AND INDUSTRY – a letter in the Lancet, July22, 2000. Peter Wilmshurst suggests that conflicts of interest in articles in medical journals are concealed because often the sums of money involved are so huge that the readers would question whether the doctor/researcher/opinion leader was expressing genuinely held views. The author says that one pharmaceutical company employs several eminent cardiologists to lecture to promote their drugs who are each receiving £3000-£5000 plus travelling expenses for an evening talk in the UK and some even have agents to negotiate their fees! The author goes on to say that it would be naïve to imagine that the size of the fees does not affect the statements of these opinion leaders/experts. It is hard to imagine too that these are not the same experts that advise the MCA/CSM!

IN THE FALL OUT OF THE TROGLITAZONE WITHDRAWAL – the New York Times exposed that the manufacturers of troglitazone for Type 2 diabetes, eventually withdrawn because it caused liver failure, paid speaking fees to 300 endocrinologists and GPs across the US to market/sell it to the medical profession. No doubt these were leaders in the field that other doctors would respect. Furthermore Dr R C Eastman, the FDA adviser that oversaw the drug through its trials, was put on the payroll of the manufacturers!

**Why is all this important to us?**
'Human' insulin provides a perfect example of the answer. We want animal insulins to continue to be available for those who need them and recognition that some people requiring insulin have adverse effects to 'human' insulin. But for reasons that remain a mystery, although not beyond our imaginations, there has been great resistance to any criticisms of 'human' insulin by manufacturers, the medical experts, diabetes organisations and these government departments. But our battle is not being fought on a level playing field!

We, the patients, have to argue our case with the MCA but without access to information about the original trials, their size, the type of participants, where and by whom they were carried out, the adverse reaction reports and the drug company responses to them. This makes it an impossible task but just think how different the case would have been if we had access to all the information held by the MCA. It was set up for our protection, not the protection of industry or anyone else, but amazingly it does not have to justify or demonstrate to anyone the basis for its decisions.

In our case the MCA does not have to disclose its reasons for maintaining that 'there are no concerns about the safety of human insulin' and nor does it have to expose the names of their advisers and whether they had any conflicts of interest. We are supposed to be just compliant believers in their decisions – sorry but the world isn't like that anymore! When the CSM was set up in 1968 maybe, but things have moved on and the pharmaceutical industry has become one of the most powerful industries in the world - we all know what power does!

We, the patients, have moved on too, with governments encouraging us to take greater responsibility for our own healthcare. But this also means that we are more aware, we require more information and we will not lightly accept statements without supporting evidence, especially if these contradict our own experiences.

Of course, we do not know that owning shares or receiving financial benefits from industry influences decisions made by the experts but it could happen unwittingly [and we do not know that it happened with 'human' insulin]. But these are intelligent people, why do they think that drug companies give them money? If the companies did not believe it gave them influence, they would not do it. It has to be remembered that the drugs under consideration by these MCA experts have the potential to threaten lives or have devastating side effects but they also have the potential to make billions of pounds for industry.

The drug companies say there is no alternative to the present system - because there are so few experts available that they are in constant demand by both Government and industry. This is not just a case of justice being done but of justice being seen to be done and there are alternatives. If experts want to act as MCA advisers then they should sell their shares so there is not even the potential for conflict of interest. As for those who accept payments of various sorts - they could always refuse to accept drug company money, it is on top of their salaries when all is said and done!

## Driving Update

On January 1st 1998 driving regulations changed for EVERYONE preventing people from driving category C1 [lorries and light vans between 3.5 and 7.5 tonnes] and D1 [9 -16 seat minibuses] vehicles on their CAR driving licence. This comes into effect on renewal of the car driving licence. The problem for people with a medically restricted licence issued for a maximum of 3 years, is that they will be affected much sooner than people holding a normal licence. People using insulin are not being singled out – there are about 10 other conditions that have restricted licences, but the regulations may put them in the position of losing their jobs if it is impossible for them to drive a smaller vehicle.

The European legislation allows for 'exceptional cases' to be considered but drivers must meet the higher medical standards that have been applied to professional HGV drivers since 1991. This is largely a UK problem because the other Member States had tighter regulations anyway with no drivers, with or without diabetes, receiving a CAR licence to drive C1 and D1 vehicles.

The UK government was advised by its panel of diabetes experts and their decision was based on studies showing that insulin treatment produces a significant risk of hypoglycaemia that can lead to loss of consciousness or diminished judgement. Hypos without warnings can occur and a number of accidents have directly resulted from this.

In September 1998 the government introduced revised legislation:

- The ban on D1 vehicles remains. (Minibuses with 9-16 passengers)
- The exceptional case basis only applies to drivers of vehicles EMPLOYED in this work. This will only be granted after a rigorous medical check.
- No new drivers will be allowed to drive C1 and D1 vehicles with or without diabetes.

On May 3rd 2000 Lord Whitty, Minister of Roads, announced that the government will review the scope for more individual assessment in the licensing regime for drivers of light vans and lorries [category C1 vehicles].

The latest announcement is a welcome one but Lord Whitty was correct when he cautioned that individual assessment would not necessarily lead to larger numbers of people being permitted to drive. Individual assessment will give insulin treated people the feeling that

they are not being unfairly treated. As people living with diabetes, we recognise the dangers - insulin treatment may cause hypoglycaemia, today's treatment of aiming for near-normal blood sugars increases the risk of hypoglycaemia and some people have intermittent loss of warnings. This is also recognised in the US where

the Federal Highway Administration has prevented people who use insulin from driving commercial vehicles although it did temporarily waive commercial restrictions for some insulin treated people providing they met certain medical standards. In Canada from 1987 people with Type 2 diabetes but only some exceptional cases with Type 1 diabetes have been permitted to drive trucks under certain conditions but not buses minibuses or emergency vehicles.

New Research published in Diabetes Care [Vol 23: No 5 May 2000]

An analysis of crash risks among diabetic truck-permit holders was carried out in Quebec by looking at the records of 13,453 permit holders between 1987 and 1990. People with Type1 and Type 2 diabetes were involved because treatment of Type 2 with sulphonylureas can cause hypoglycaemia. Additional health information was obtained and a telephone survey collected information on driving patterns. This applied to people driving Class 1 [articulated trucks] and Class 3 [single unit trucks] looking at 3 groups – those with complications, those without complications and those treated with insulin.

In assessing the results it is important to take into account that there are fewer professional drivers in both articulated and single unit truck classes with diabetes with complications and considerably fewer taking insulin. The results were as follows:

- articulated truck drivers - the 3 groups with diabetes did not differ in their risk ratio for crashes from the healthy group.
- single unit truck drivers - the people without complications had a higher risk ratio of crashes than the healthy group, this applying to both Type 1 and Type 2 people with the same diabetic condition in this group.

The authors offer possible explanations of higher risk ratios for single unit truck drivers:

1. The most obvious is that drivers of articulated trucks are subject to more stringent medical requirements than single unit truck drivers and therefore are selected out initially. The crash risks may also be underestimated because of self-selection with the more severely affected people choosing not to drive or to restrict their driving.
2. The work environment for single unit truck drivers seems more stressful – they are more likely to be driving on busy urban streets with parking difficulties than are articulated truck drivers and they have a tighter time schedule.
3. They spend more time handling goods and have a less regimented work situation than articulated truck drivers.

The authors recommend that the results warrant further investigation and the apparently non-significant differences in healthy groups and articulated truck drivers should not be regarded as reason for relaxing the current medical restrictions.

## 'Human' And Animal Insulin Compared

A review by Professor Rhys Williams et al and funded by the British Diabetic Association. Three versions but do you know which version is the real one?

Well we do! But we must not fall into the trap of throwing the baby out with the bath water, all versions of the Review offer firm evidence to support the experiences of patients having problems with hypoglycaemia/loss of warnings when using 'human' insulin.

- 7 out of 37 double-blind randomised controlled trials [the best quality research] show increases in frequency and/or reduced symptoms of hypoglycaemia. So nearly 20%, or a fifth, support

the experiences of many patients over nearly 20 years.
- The Review says that the evidence is unsatisfactory in many ways and that well-documented, rigorously analysed qualitative descriptions of patients' experiences are almost completely lacking and that this is a largely unexplored area.

It can no longer be said that there is 'no scientific evidence, to support patients' experiences and presumably this has resulted in the change in the BDA/Diabetes UK stance in their Press Release dated 11th July 2000:

*"We know from patients experiences that some people with diabetes cannot manage their condition with 'human' insulin, this report confirms that it is vital for these people to have access to 'animal' insulin. Greater recognition is needed among those prescribing insulin that animal varieties may be the most suitable treatment for some people with diabetes. Unless this is done the health service risks failing a significant minority of people with diabetes. Diabetes UK is committed to ensuring that animal insulins remain available to those who need them."*

We hope that this is a meaningful statement on which they will act and not just a simple matter of seeking assurances from manufacturers. Diabetes UK is ideally positioned to take positive steps to act on behalf of all patients who are denied information about and access to animal insulin because their doctors and healthcare professionals are still refusing to believe patients' experiences. Although their press release says that the Health Service risks failing this group of patients, I am sure they realise that in fact it will be the physicians and healthcare professionals who deliver treatment that risk failing this group of patients.

Late News – Disappointingly, the Autumn edition of Diabetes Update, the Diabetes UK publication for GP's and healthcare professionals, does not take this firm stance, it follows their usual line of 'animal insulin must remain available for those who need it.' However, Prof Rhys Williams is quoted as saying: "If science can't prove something, that's not proof that it is not there." How long have we been saying this!!!

But now to the three versions of the Review…

The original version was carried out under the auspices of the Cochrane Diabetes Group [CDG] led by Professor Rhys Williams, which subsequently collapsed and has since been re-formed in Germany.

Just to remind you, the Cochrane Collaboration carries out systematic reviews of randomised controlled trials in various areas of medicine and so provides reliable evidence from research to inform decision making by doctors and patients. Cochrane Reviews have a protocol [design] that usually includes the title, the aims, the methods and the outcome measures to be looked at. The outcome measures are important because they include all aspects of a treatment and so demonstrate whether there are any beneficial effects from a newly introduced treatment compared to the older one – in this instance, the new therapy being 'human' insulin compared to the older therapy with animal insulin. This is just what people treated with insulin needed to settle the ongoing debate.

This sounds just fine and dandy, so what went wrong?

- IDDT, invited to comment on the original protocol, said that it was too narrow, only covered hypoglycaemia and not all the other reported adverse reactions to 'human' insulin. Our comments were virtually ignored, although the title did include 'other side effects'. Alarm bells started to ring at this stage – why would an independent group of researchers not want to look at the whole issue?
- We then discovered that the Review was to be funded by the British Diabetic Association [now Diabetes UK]. We objected to this as we believed that neither the BDA not IDDT should fund this review because if the Review was to have any value, it not only had to be independent and unbiased, but also had to be seen

to be independent and unbiased. I travelled from Northampton to Leeds to meet Rhys Williams but failed to influence either the protocol or the source of funding, but then I was only given half an hour! The alarm bells became louder and I had a feeling of having been here before with the Posner Report, again commissioned by the BDA, but never published.

- IDDT pulled out of further involvement with the Review with the intention of making formal comments and criticisms once the completed Review was published on the Cochrane database. But before this could happen, the Cochrane Diabetes Group collapsed and the Review was never published on the Cochrane Database. Alarm bells became louder as, once more, the control for release of information about 'human' insulin rested with the BDA and out of our control or the control of Cochrane.

**So what did the BDA/Diabetes UK eventually do with the Review?**
May 1999 - it was presented at the BDA Medical and Scientific Conference by Professor Williams. The presentation was the 1998 completed Review, albeit not the review we would have liked, but it was the complete review.

June 2000 – The Cochrane Review was put on the BDA/Diabetes UK web site. A visit there showed that this was a different version and the section about deaths associated with 'human' insulin had been omitted.

June 2000 – Diabetic Medicine, the BDA journal for professionals, published yet a third version. We fully understand that this had to be a summary of the original 1998 version but what is published is not a summary - it bears little resemblance to the original 1998 version. The alarm bells were replaced with anger and a little voice saying 'I told you so, I told you so, you knew it would happen, you've been here before'.

**What are the changes and why are they significant?**

- The title has been changed from "To compare 'human' and animal insulin in people with diabetes mellitus in terms of symptoms associated with hypoglycaemia and other side effects" to "Hypoglycaemia induced by exogenous insulin – 'human' and animal insulin compared." The omission of 'other side effects' means continued failure to address the other categories of adverse reactions to 'human' insulin so that patients and doctors are still not in a position to make truly informed decisions about which type of insulin to use.
- The aims have been changed to "examine whether published evidence suggests a difference in frequency and awareness of hypoglycaemia induced by 'human' and animal insulins." In addition to the omission of the 'other side effects, there is one very significant little word in the Diabetes Medicine version –to examine 'published' evidence. The original aims were to look for ALL evidence and which included searches for unpublished studies that may be held by Novo Nordisk, Lilly and/or regulatory bodies but remain unpublished for some reason.
- The outcome measures have been changed to "frequency, severity awareness and symptoms of insulin induced hypoglycaemia." so excluding the 9 other outcome measures that were in the original Review. These were:

Glycaemia control and ketoacidosis

Counterregulatory hormone measurements and other appropriate measures

Neuropsychological tests

Patient satisfaction and quality of life

Any other side effects

Associated morbidity – injuries and convulsions

Hospital admissions

Mortality

Financial costs

By removing these outcome measures in the Diabetic Medicine version and indeed, by not fully addressing them in the original Review, there is a basic failure to address all aspects of the healthcare intervention with 'human' insulin that is expected in a Review. [Intervention is research speak for treatment or insulin therapy in this case.] If all these outcomes had been looked at, then we would have had a great deal more information and their inclusion would have shown whether there are any positive effects of therapy with 'human' insulin. Even if searches of the literature find no information either because it is unavailable or because no work has been carried out in this area, then this should be reported in the Review because missing information can be vital for informed decision making by both patients and doctors.

For example, only one study was found that compared 'human' and beef insulin, the rest all compared 'human' and pork insulins [very convenient as pork is a nearer match to 'human' insulin and so one would expect fewer differences to show up]. One study is not enough to provide reliable evidence and it is certainly not enough for doctors, the FDA or anyone else to tell beef insulin users that they can easily change from beef to 'human' insulin without problems. Such statements are totally unsupportable and yet this is exactly what is happening right now following the withdrawal of beef insulin in the US. Turning the tables somewhat, there is no scientific evidence for doctors, drug companies or regulatory bodies to make such claims and not only is this unacceptable but it puts into question their judgements and even their motives.

In the year 2000, even patients have heard of evidence based medicine! At risk of stating the obvious, it is medicine based on evidence and the value of all the versions of this Review is that it demonstrates that decisions about type of insulin treatment are not based on reliable scientific evidence. A bold statement maybe, but an undeniable one.

There are some very serious questions that arise:

Who decided to omit the section about deaths in the web site version, Professor Williams et al or the BDA as funders of the Review, or …..? Why was it omitted? The defence that 'it will alarm patients' is no longer acceptable and assumes a paternalism that is unnecessary, insulting and unfair to patients, many of whom want to be able to make truly informed decisions about their treatment.

The version in Diabetic Medicine raises even more serious questions

- Why was this changed so that it was almost unrecognisable as the same Review?
- Why were all the other side effects excluded from the review?
- Why were 9 outcome measures omitted?
- Perhaps most importantly, who decided to do all this and why?

A letter asking all these questions has been submitted to the editor of Diabetic Medicine which also points out that patients who have suffered as a result of using 'human' insulin are already deeply suspicious and this latest situation confirms that they have good reason to be!

On a personal note, I cannot describe my frustration and anger at yet another fudge of the 'human' insulin issue especially as the alarm bells were ringing all along and I would have wagered my last bean that something like this would happen. I've been around too long to labour under any illusions that suddenly we were going to be allowed a straightforward uncomplicated bit of truth! My anger will not disappear and I shall be like a dog with a bone - I will not leave it alone. There are moral and ethical questions that must be raised, even if those who can provide the answers choose not to. This is one 'fudge' too many! The 'human' insulin saga has understandably left many of us deeply suspicious, but the public has to be able to trust research, those who carry it out, those who publish it and those who fund it. Three versions of one Review make this very difficult! Why did anything from the original Review have to be changed? Where is the gain and for whom?

# Stocks Of Animal Insulins In Hospitals

Many people have expressed concerns about their insulin treatment if they are in hospital and this was very apparent at lasts year's IDDT Annual General Meeting. The concerns were that they were often changed to 'human' insulin against their wishes, while they were inpatients and that they had to have 'arguments' to be allowed to use animal insulin, even their own supply. The major worry was that if they entered hospital in emergency and unconscious, then 'human' insulins may be administered even though their records showed that they use beef or pork insulin and they had previously reported adverse reactions to 'human'. These worries are real as significant numbers of people have already had these experiences and at the AGM the Trustees promised to take some action on what appears to be a nation wide problem.

In April 2000 we wrote to the chief executives of all hospitals in the UK making the all the above points plus a few more:

- The lack of availability of animal insulins within hospitals when patients enter in emergency or for a pre-planned in-patient stay and/or the refusal to allow them to use their own animal insulin is very distressing for the patient and their family carer.
- CP Pharmaceuticals Ltd, manufacturers of beef and porcine insulins assure us that, apart from weekends, wholesalers could supply any hospital with the necessary animal insulin within 4 hours. Yet the 15-20% of people who need animal insulins are often unable to receive it and are transferred to 'human' insulin against their wishes.
- As this situation appears to be getting worse, IDDT has no alternative but to draw attention to the need for hospital pharmacy departments to stock animal insulins to help to avoid a potentially dangerous situation for the patient and one that could be uncomfortable for the hospital. The Patients' Charter gives people the rights to choice of treatment and this group of people in conjunction with their doctors, have already made the choice to be treated with bovine or porcine insulin.

**Responses from Hospitals**

Of course we didn't get many! However, the responses we did receive varied greatly with major successes in Northern Ireland – both Newry and Mourne District Council and Ards Borough Council wrote to tell us that at a meeting they had agreed to support our call for animal insulins to be stocked in all hospital pharmacy departments. The Directors of Administration have written letters to Health and Social Services Boards and to the hospitals and Community Trusts. Then when looking through press cuttings, I found an article in the Newtownards Chronicle and here is an extract:

**Hospitals urged to maintain animal insulin.**

Strangford Assembly member Jim Shannon is urging hospitals across Northern Ireland to maintain their stocks of animal insulin. His call comes in the wake of a report from the Insulin Dependent Diabetes Trust which claims that this option is being ignored. ...Mr Shannon commented that hospitals using only human insulin appeared to be ignoring the plight of up to 70,000 people and said " It is becoming clear that more and more hospitals are not maintaining their stocks of natural insulin and this has serious implications for the patient who may be admitted to the A&E department" ….He said " It appeared that hospitals were adopting a cavalier attitude to the question of insulin and he indicated that he would be writing to the Department urging that the situation be addressed immediately."

Well Done, Mr Shannon!

But what about the rest of the UK?

In most cases, the Hospital Chief Executives referred our letter to the hospital pharmacist and this is where the variety of attitudes showed up.

Some of the good comments:

- Our hospital does keep a limited range of animal insulins and we are always willing and able to obtain others from wholesale

suppliers when necessary.

- Thank you for your informative letter, we will keep it as a service of reference. We do not have an A&E department and the majority of our admissions are pre-planned. The hospital always orders and supplies the same medication for patients and would not change the type of insulin without consent.
- All hospitals in our region stock considerable amounts of animal insulins which we use for a considerable number of patients.
- We stock a full range of animal insulins and are fully aware of the problems because one of our pharmacists has diabetes!

A mixed response:

- From a consultant: I am an enthusiastic user of animal insulin in the outpatient setting. I think your letter is over the top….I consider that it does no harm whatsoever for an individual to go on to 'human' insulin temporarily when they are in hospital and then later on return to animal insulin if they so wish. [Tell that to the patients who end up staying in hospital longer because of the severe hypos they experience while in there!]

The worrying responses:

- For a pre-planned admission patients should bring their insulin with them. It should be understood by patients that 'human' insulin is not poison. [Patronising or what?] The patient is expected to take reasonable care of himself. It must be recognised that non-human insulin users are a 'special' group receiving 'special' medicine who should take extra precautions. [This is a revelation! What excuse next?]
- No hospital can be expected to stock every preparation of medicine. Naturally wastage must be minimised ….for hospitals to stock more and more medicines 'just in case' inevitably leads to wastage and NHS money being tied up in stock and written off when medicines expire. [Maximum of one vial each of 7 animal insulins at wholesale price with a shelf life of 2 years – dear me!]
- Using the wholesaler emergency service that you have been advised about by CP Pharmaceuticals involves our organisation in considerable effort and expense.[A telephone call?]

"Diabetic discharges himself after mix up" - as if to prove the point, on July 6th a little article in the Woking News reported that a 78 year old man entered St Peter's Hospital for an operation taking with him his own pork insulin and a list of his medications from his GP. He says "The next morning I was put on an insulin drip. Later I had a bad hypo and after a panic session I was revived. I asked the doctor if it was possible that I had been given 'human' instead of pork insulin and I was told not to worry." The following day he suffered a hypo again and he queried the type of insulin being used, with no response. The next morning he asked a nurse if the drip contained 'human' insulin and she said it did. He asked for the drip to be removed and discharged himself! The hospital is to hold a full investigation – perhaps they should look in the bins to find the letter from IDDT advising them of exactly this problem!

**Taking your own insulin with you – not always the answer!**

Since carrying out the mailing to hospitals, we received a very distraught call from the wife of one of our members requesting that we once again raise this whole issue in the Newsletter so that others do not have the same experience that she and her husband had. Mr X went into hospital for major heart surgery and the hospital insisted that Mrs X went home to collect his insulin so that this could be used in the drip. Mrs X returned to the hospital with the insulin that was immediately put in the drip reservoir by a nurse, despite Mrs X's protestations. No one listened to her and Mr X remained on this insulin for several days and verging on unconsciousness for most of the time. Hardly surprising, his normal insulin regime is twice daily beef Lente – a long acting insulin definitely not to be used for continuous administration in a drip. Mrs X has now seen a solicitor…

**From the General Medical Council [GMC]**

We sent a copy of our letter to the GMC for their information and their general advice is: "We always expect doctors to act in the best interests of their patients and to listen and respect their views and

their right to be fully involved in decisions about their care. We also expect doctors to be satisfied that, wherever possible, the patient has understood what is proposed, and consents to the treatment.

We advise that in an emergency, where consent cannot be given, the doctor provides medical treatment to anyone who needs it, provided the treatment is limited to what is immediately necessary to save life or avoid significant deterioration in the patient's health. However, the doctor must still respect the terms of any valid advance refusal which he/she knows about or has been drawn to his/her attention. The patient must be told what has been done and why as soon as he/she is sufficiently recovered to understand."

This means that if you needed insulin in emergency, for example if you were hyperglycaemia, then 'human' insulin could be administered to save your life or prevent further problems and none of us would disagree with this, assuming your usual animal insulins were not available. But once recovered, you should be told of this and your wishes to return to animal insulin should be respected. This GMC advice makes it clear that you should have it recorded in all your medical notes that you do NOT want 'human' insulin administered – hence you have complied with the advance refusal referred to.

IDDT supplies stickers for your notes saying "This patient does not give consent for 'human' insulin to be administered." Contact IDDT, PO Box 294, Northampton NNI 4XS, telephone 01604 622837 or e-mail stickers@iddtinternational.org

## What The Papers Say

Daily Telegraph, 11 July, 2000 - Babies of older mothers more at risk of diabetes

A study published in the BMJ has found that there may be a link between the increase in childhood diabetes and the age at which mothers are having their first baby. The risk of diabetes developing increased by 25% for every 5 years of the mother's age so that the first born child of a woman of 45 was three times more likely to develop diabetes than the first born child of a woman of 20. The researchers suggest the cause could be that in the older mother, the baby's developing immune system is more likely to be affected. The age of the father may also be implicated as the study showed that the risk increased by 9% for every additional 5 years of his age. Apparently, between 1970 and 1996 the population of children born to mothers aged 30-34 increased from 15% to 28% and estimations are that childhood diabetes is increasing at the rate of 4% per year.

The Independent, 10 August, 2000 - Stomach virus may be linked to childhood diabetes

The most common cause of diarrhoea and other stomach bugs amongst children is a group of viruses referred to as retroviruses. Researchers in Australia have shown that there may be a link between retroviruses and children developing diabetes. Over a 6 year period, 54 babies who had a parent or a sibling with diabetes and were therefore at risk of developing diabetes, were studied. In 24 of the children who showed clear signs of developing diabetes, antibody levels in their blood went up every time they got a retrovirus infection, signalling an attack on the pancreas. After the infection the antibody levels dropped until they fell ill again. Children who did not develop diabetes showed no signs of their pancreas being attacked when they had a retrovirus infection. It is not known whether the retrovirus causes diabetes by damaging the cells of the pancreas or whether it mimics proteins in the pancreas which cause the immune system to attack the insulin-producing cells.

Researchers are now left in a quandary because it had been hoped that retrovirus vaccines could prevent thousands of children in third world countries dying from stomach bugs. But if the retrovirus does mimic the proteins in the pancreas, then a vaccine could also trigger diabetes. Retroviruses are responsible for up to 80% of childhood

diarrhoea in third world countries and two thirds of all childhood diarrhoea in the UK.

Scotland on Sunday, 13 August 2000 – Diabetes linked to the diets of mothers

Research looking at Scottish mothers and babies has shown for the first time that a pregnant woman's eating habits can affect the chances of her child developing diabetes in later life. Researchers looked at the medical records of mothers who attended Aberdeen Maternity Hospital between 1948 and 1954, which contained details of their diet, and then tracked down their children. They found a link between high intake of fat and protein [meat, fish, eggs and dairy products] and insulin deficiency in their children when they reached middle age. They think that high levels of fat and protein in the mother's diet impairs the development of the insulin producing cells while the baby is in the womb.

The Independent, 18 August, 2000 – fast-growing children face risk of diabetes

An analysis of 2,400 children has shown that children who grow quickly in the first three years of life because they are allowed to eat as much as they want are more likely to develop diabetes. The research showed that children from affluent homes are more likely to develop diabetes, as an abundance of food leads to increased growth associated with increased insulin secretion. The children at risk were heavier and taller than their peers. This could explain why diabetes is more common in affluent countries and in poorer countries the lack of food means that the children are less at risk of developing diabetes. In the UK the incidence of childhood diabetes has doubled in the last 5 years, with about 1200 children under 5 years old developing it.

# What Do Doctors, Specialists And scientists Know About bieing Diabetic?

A personal view by Shirley Stone

As with any trade –I name engineering as one – it is one thing to read a book and learn how to build a machine or repair a broken one, but when you get out in the field it is a very different story. So it is with diabetes, it is one thing to study it at college, university or elsewhere to learn about it, but to actually live with it day in and day out is something else.

I have been diabetic for in excess of 33 years and have always done my best to look after myself to the best of my ability. It seems very strange that the only times I have really 'suffered' have been at the hands of doctors who said they know best. I could write a book about my experiences with diabetes and doctors but the final 'insult' was when I was changed to 'human' insulin. I kept extremely good control on my old animal insulin and when I was changed (with no explanation from my GP as to any changes that I should or could make)I was told by the receptionist that my new prescription would appear slightly different but the insulin was just the same. She even stated that her own son was on the new insulin and didn't notice any difference. If only I had realised what was about to happen, I would have insisted on keeping to my old regime.

So started 8 years of suffering, not just the absence of warnings of hypos. I also suffered from:

- stiffness in my joints,
- permanent thrush,
- deteriorating eyesight,
- inability to walk even short distances due to circulatory problems in my legs,
- the inability to think for myself (my brain felt as though it was full of cotton wool), severe palpitations (there were times when I thought

I was going to have a heart attack it was so painful)

- last, but not least was my aggressiveness. Whilst I admit that I am an excitable person, I am not normally aggressive. However, this insulin brought out an extremely nasty reaction so that no one could speak to me without me all but screaming at them. I was not a nice person to know.

I couldn't believe what was happening to me. I had kept so well previously and although I regularly visited the doctor, he had little or nothing to say about my deteriorating health. It wasn't until I was talking to a friend who is also diabetic that everything became clear. He too had suffered at the hands of 'human' insulin and described his side effects that were identical to mine. I decided the time had come to do something about it and promptly went to my doctor. I explained my fears and worries to him and asked if I could try animal insulin again. Imagine my surprise when he readily agreed and asked what sort I would like – beef or pork? I was fully expecting a stand up fight for my right to choose but thankfully, he accepted my request.

I can only describe myself as being 'reborn' following the changeover to animal insulin. Absolutely all the side effects listed above disappeared and my husband said he was glad to have his wife back again instead of the grumpy, short tempered stranger he had been living with previously.

In my early days as a diabetic, my specialist was diabetic himself. He was so kind and totally understanding of how we felt and he always said I was one of his 'best' patients. I have since seen a doctor who thumped his desk saying I should do this and I should do that and he was quite amazed when I asked him how long he had been diabetic. His response was that obviously he was not! Need I say more! I now insist on seeing the 'man at the top' at my hospital who, whist he is not diabetic, is a little more understanding and who has praised my ability to take good care of myself. I have no signs of kidney problems or damage to my eyes.

Obviously, it makes me feel proud that I have done so well over the years, but I cannot help but wonder what might have happened if I had been forced to stay on 'human' insulin. Could it be that I might have been blind or in a wheel chair, or even worse. Thankfully I will never know.

I guess what I am trying to say is that if the people who invented 'human' insulin and those that decree 'all diabetics should take this new and exciting product' were diabetic themselves and suffered the way we have, would they still feel the same? Would the people in charge at Novo Nordisk, Lilly and the other manufacturers of 'human' insulin still decree that 'human' insulin is the answer for everybody? I think not.

I can only say a big thank you to everyone at IDDT for being there, listening and acting on our behalf. I would say thank you to CP Pharmaceuticals for manufacturing the very necessary animal insulin. Please, please keep up the good work.

## Latest On Inhaled Insulin

A Canadian company, Generex Biotechnology, are developing an oral insulin spray, and now have an agreement with Eli Lilly that will market it. Lilly will pay for the remaining clinical trials and getting it through the regulatory procedures and Generex will receive initial fees and milestone payments. This inhaled insulin is absorbed through the inner cheek walls whereas the Novo Nordisk version is absorbed by the lungs.

## Information For You

**NHS Direct Wales**

NHS Direct Wales became available to residents of Mid and South Wales on June 13th this year and the second phase to cover North Wales will be available by the end of October. The service in Wales aims to provide people with advice and information about health, illness and the NHS. Highly experienced qualified nurses from a range of different clinical backgrounds give people immediate information and advice on what to do when a caller has a health worry, at any time of the day or night. The service is bilingual and confidential.

There is a single national number to contact NHS Direct, 0845 46 47.

'WOMEN'S HEALTH' is a voluntary independent organisation that provides information and support to women on a variety of health issues affecting women. It is a confidential service and their Health enquiry line is available between 10am and 4pm everyday except Tuesday. Contact Women's Health,
52 Featherstone Street,
London
EC1Y 8RT.
Tel 020 7251 6580
e-mail womenshealth@pop3.poptel.org.uk

## Diabetic Commonsense - balance and choice

**A personal Account by Beatrice Reid**
Beatrice Reid has had diabetes for 70 years and so she must have been doing something right all these years! Her book about her commonsense approach to living with her diabetes and the management of it, has been greatly appreciated by many of those who received it in the August mailing. Beatrice published the book herself and it is enticing reading especially as she offers a 'Health Warning' on the first page:

"This little booklet is written for ordinary people: diabetic specialists would be well advised to steer clear of it. My commonsense approach might disturb the medical fraternity, for it will challenge the assumptions of recent practice and expose folly that can result from behaving towards diabetics as if they were scientific experiments instead of human beings."

Copies of Beatrice's book are available free of charge from IDDT, PO Box 294, Northampton NN1 4XS Tel 01604 622837

e-mail enquiries@iddtinternational.org

## IDDT Parents' Supplement

Published in August 2000, includes articles for parents of children and teenagers about diagnosis, growing up, letting go. The central feature is an article by Dr Clare Williams entitled 'Teenagers with Diabetes' which looks at the role of parents in helping their teenagers to become independent and the differences experienced by parents of boys and of girls. Free copies of the Parents' Supplement are available free from IDDT, PO Box 294, Northampton NN1 4XS Tel 01604 622837
e-mail enquiries@iddtinternational.org

## SOS Talisman Jewelry

Tailsman Jewelry is now available ONLINE. This jewellery incorporates a capsule containing the wearer's medical and personal information in case of accident or illness. Visit www.sos-talisman.com

## Do Kilograms Mean Much To You?

If you are my generation kilograms [kgs] probably mean very little as I was brought up with good old pounds and ounces. But when somebody told me the other day that their baby weighed 4 kgs, I thought it was time I learnt what this meant!

Apparently, one pound equals 0.45 kgs, so in future I might remember that just under half a kilogram is equal to one pound. I still think in terms of feet and inches but I can remember that a metre is just over a yard and so a foot is about one third of a meter!

## Don't Forget To Order Your IDDT Christmas Cards!

Please help us to help you by ordering some of our Christmas cards now.

If you have mislaid the details and order forms, give Kirsty at IDDT a ring on 01604 622837 or e-mail cards@iddtinternational.org but of course you can still contact us in the good old-fashioned way by post to IDDT at the usual address!

## Heinz 57 - A Variety Of Information

**Depression may also increase heart disease risk**
If you are depressed perhaps this is just what you didn't want to know! A study

[ref 1]carried out in the US has found that people with diabetes who are also depressed are more likely to have heart disease. The researchers investigated 657 men and women with diabetes for diabetes complications and risk factors. They found that symptoms of depression were quite strongly associated with an increased risk of heart disease and heart attacks. They also found that high blood pressure, low cholesterol levels, high white cell counts and kidney disease were also risk factors for heart disease.

Ref 1 Atherosclerosis 2000; 1489: 159-9

## More About Eating Disorders

A study published in the BMJ, 9.6.00, showed that teenage girls with diabetes are twice as likely to suffer from eating disorders as non-diabetic girls of the same age. Experts warn that intensive care treatment, which can cause weight increase, may be a contributory factor in the higher rates of eating disorders amongst young women with diabetes. They also warn that girls with diabetes and eating disorders are at greater risk of the early complications of diabetes with a threefold risk of permanent eye damage.

1545 Canadian girls between the ages of 12 and 19 were studied and they found that girls with diabetes were 2.4 times more likely to have an eating disorder. 10% met the medical criteria for diagnosis of an eating disorder compared with 4% of young women without diabetes. Even more worrying is that a third of the girls admitted to binge eating and 11% said they had either under dosed or stopped taking their insulin at some stage.

Jenny's comment – now that my daughter is well and truly adult and we have been able to talk about the past, she has told me that sometimes she under dosed and sometimes did not take her insulin at all. While I was suspicious at the time, I did not actually know this was happening. If I had, I probably would not have classified them

as an ‘eating disorder’, but they are and they need addressing in the care of teenagers with diabetes, especially now there is concentration on tight control.

## Anger - Worth A Thought

The Observer magazine published 21 May 2000 had an interesting snippet that those of us who tend to get angry perhaps should remember. Apparently the University of North Carolina has released a report detailing links between heart attacks and anger. This is something that has been said for years but this study has been rigorous in trying to find out if this is historical folklore or fact.

13,000 people with normal blood pressure were looked at over a 6year period, 256 of whom had heart attacks. People with diabetes, high cholesterol and excess weight were looked at separately. The study concludes that a person that is prone to anger is three times more likely to have a heart attack or sudden cardiac death than those who are less prone to anger and this is especially true in middle aged men and women. It also showed that anger, anxiety and depression are likely to have a detrimental effect on health.

The article also quotes an American psychologist Leonard Ingram as identifying four main keys to managing anger:

- Not misinterpreting other people’s behaviour to you as hostile.
- Identifying factors in your upbringing which predispose you to anger.
- Learning ways to express legitimate anger.
- Forgiving those who hurt you.

Jenny’s comments – I think this was written as a warning to people like me! This whole ‘human’ insulin issue frequently makes me and many others angry but perhaps IDDT is our way of managing that anger! It is certainly legitimate anger.

## Reliving Joint Pain - you should be aware!

Drugs often used to relieve arthritic joint pain [and therefore often used by people with diabetes with painful neuropathy] are called non-steroidal anti-inflammatory drugs, NSAIDs for short. Ibuprofen is just one common example of this type of drug. NSAIDS come in tablet form but also in creams, gels, foams and sprays, referred to as topical NSAIDs because they are applied to the skin surface.

According to Health Which, the prescriptions for topical NSAIDs cost the NHS nearly £20million in 1998 and there is an additional use because this figure does not include those bought over the counter. The sister journal, Drugs and Therapeutics Bulletin [1999;37:87-88] looked at how effective topical NSAIDs are in relieving chronic arthritic joint pain and their results produced a recommendation that topical NSAIDs should not be prescribed on the NHS for the following reasons:

There was little reliable evidence about where the products go in the body after they are put on the skin.
It is not known how well topical NSAIDs work when used in the long term or how likely they are to cause serious side effects because of absorption into the body.
What evidence is available suggests that they might be slightly better than a placebo [dummy] preparation at relieving joint pain.
There is no reliable evidence that they are more effective than standard treatments for joint pain, such as paracetamol or NSAIDs taken by mouth or other topical preparations called rubefacients that work by irritating the skin over the painful area.

It is worrying that not only is the NHS paying a high price for these drugs, as are people purchasing them over the counter, yet they are

not proven to be effective and even worse there is no evidence that they are safe for long term use.

## A Bit More About HRT

The decision for using HRT is one that many women find difficult and women with diabetes are no exception – in fact they probably debate this issue even more because they have their diabetes to take into account as well. We have covered this in previous Newsletters and tried to give the evidence that is available but there is no clear cut answer. The results of a recent large trial using patients randomised to either HRT treatment of a placebo [dummy pill] has shown that HRT with oestrogen and progesterone increases the risk of thromboembolism [blood clot] almost three-fold in women with coronary heart disease. [Ref 1] It also showed that the risk was greater in women with 'lower extremity fractures'. This study was general and not specific to women with diabetes but women with diabetes do have a greater incidence of heart disease than the general population and so it is information that is worth having.

Ref 1 Ann Intern Med 2000;132:689-96

## From Our Own Correspondents

**Lilly confusion**
Dear Jenny,

So I am not paranoid after all, the packaging of Humalog and the Humalog Mix 25 is disgraceful! My son Scott has been on this newer insulin for about 5 months now and I was stunned by the complete lack of thought that must have gone into the packaging of this product. This is by and large a young adults insulin and colourful well identified boxes cannot be that hard to produce. In fact, if Lilly want to pay me I will do it for them! If you have not seen these boxes, they are very similar and both are coloured in a boring brown colour. The packaging shows a total lack of thought into the marketing of this product and I personally would sack the team that approved this very poor design.

Anyway the insulin may be faster acting but so far we have seen little improvement in roving blood sugars. Let's get the glucose watch sooner rather than later…

Philip Johnston
Glasgow

**Comment**: The colours of insulin packages are standardised, supposedly to help people differentiate between the various insulins. This obviously didn't work with the two types of Humalog. Interesting though that Scott has had no improvements with his roving blood sugars since trying these newer insulins – rather ties in with the marketing approval information and the subsequent research comparing them to 'human' insulin but research has shown a reduction in night hypos for some people but not without subsequent highs during the night and more hypos in the evenings.

**I just wanted you to know…**
Dear Jenny,

My husband is a member of IDDT, he will be 70 years old in August and has been a diabetic on animal insulin for 65 years. When visiting the hospital 3 weeks ago, the doctor told him that he had never known anyone that has been on insulin this length of time. Some years ago he was told never to go on to 'human' insulin. I just thought this may be of interest.

Mrs B.J.
South East

**I stuck to my guns!**
Dear Jenny

After reading your article on 'human' insulin in our local paper, I felt I had to comment. I have been a diabetic for 30 years and some years ago my GP started me on 'human' insulin after I had been on pork insulin for several years. In a short time I began to feel ill and after several weeks revisited my GP and told him I thought the insulin was to blame. He said it was my choice and put me back on pork insulin.

In 1995, whilst my own doctor was on sick leave, his partner referred me to the Diabetic Unit at my local hospital because my blood sugar was high. The Nurse assigned to me said that my troubles would be over if I switched to 4 times a day pen injections and it was not until I received the pens that I realised that I could only use them with 'human' insulin.

I complained and was told that 'human' insulin was perfectly safe and that it gave better control. I began the new insulin in August 1995 and within days I felt ill and started to suffer from depression. I saw my own GP who referred me back to the hospital where I was told that I was over excited and had listened to hysterical gossip. I stuck to my guns and insisted on returning to pork insulin but I was to suffer depression for the next three years.

Imagine my horror in December 1999 when, on visiting the Hospital Clinic, I saw a new doctor who urged me to take 'human' insulin as he said it was better than pork insulin. I said 'no way' and had quite an argument with him.

I cannot understand why hospital staff are promoting this insulin as it obviously does not suit everyone. I only hope that pork insulin will continue to be available.

Mrs C.E.
Midlands

**Jenny's comments** - this is an all to familiar story to IDDT. The positive bit in all this is the reaction of the GP initially – he listened and believed Mrs C.E when she told him that her problems had started after the change to 'human' insulin. He also told her the decision was hers, so acknowledging that she did have some rights in her own treatment decisions.

## Tit-Bits

Guinea pig, but not the human kind! Several papers report the story of Squeak, a guinea pig diagnosed with diabetes after showing the classic symptoms of thirst [and a permanently wet bottom in his case!] The 3-year-old has to have twice daily injections of insulin, tablets and a special diet. Apparently he is very brave and very healthy. But it gets better…

Harry, a six-year-old monkey at a sanctuary in the West Country, has diabetes and has one daily insulin injection. Unfortunately his diabetes has caused cataracts. Harry has difficulty getting around and he is too frightened to be with the other monkeys, so has to live on his own! Staff at the sanctuary are trying to raise £1,250 for Harry to have laser treatment to hopefully give him back his sight – the first time this will have been performed on a monkey!

Dundee leads pen use - the Dundee Evening Telegraph reports that there are over 2050 people in the area using insulin, 73% of whom are described as 'leading the way by using modern insulin pens'. This compares with 43% in the rest of the UK. [I cannot help but comment that the choice of injection device is with the patient and not everyone wants to use a pen and not everyone can obtain their brand of insulin in a pen!]

Breast feeding – during National Breast Feeding Awareness Week in May there was a great deal of publicity about the benefits of breast

feeding. One of the advantages used in their campaign was that breast fed babies have a lower risk of eczema, asthma, wheezing and insulin dependent diabetes and may be at lower risk of cardiovascular disease in later life.

Perk of the job - the Observer, July 9, 2000 reported that up to a million NHS workers are routinely jumping the official waiting lists for their own treatment at the expense of ordinary patients. Hospital staff get the initial consultation and surgery quicker and are far more likely to be treated by a senior consultant. But doctors admit that avoiding delays and getting first class treatment is the last perk of working for the NHS, maintaining that it is a 'gentleman's agreement' because it keeps them working. Queue jumping techniques include cancelling operations for other patients, opening operating theatres out of hours or simply claiming that their clinical condition is far more urgent than it really is. The Department of Health has condemned it as 'totally unacceptable'.

## Reminders

**Novo Nordisk to remove lentard**
Just to remind you that in March this year Novo Nordisk announced that they will be withdrawing Lentard from the UK by mid 2001. Lentard is a 30% pork /70% beef mixed insulin and there is not an equivalent insulin available from other manufacturers. However, looking at the action profiles of all the available insulins, beef, pork and 'human', Hypurin Bovine Isophane appears to be the nearest matching insulin. The peak of action of them both starts at about the same time and the main difference appears to be that duration of this peak is shorter in the Hypurin.

If you are taking Lentard, knowing that it is being discontinued will give you time to consider all your options, discuss them with your doctor and to changeover at the best time for you, which is not always when you can no longer get supplies! For instance, it is not a good idea to change insulins just before you go on holiday or when there is some other disruption to your life.

## Soft Drink Alarm

Pepsi-Max sold in the UK [and all other countries except Canada] is normally 'sugar free', but there have been imported versions of it for sale which contain sugar. This imported can from Canada is almost identical to the UK 'sugar free' cans. Trading standards across the country have been alerted and warn people with diabetes to be particularly careful to read the labels of imported products.

**If you would like to join IDDT, or know of someone who would, please fill in the form (block letters) and return it to:**

**IDDT**
PO Box 294
Northampton
NN1 4XS

Name: ——————————————————————————

Address: ——————————————————————————

——————————————————————————

Postcode: ——————————————————————————

Tel No: ——————————————————————————

## From Your Editor – Jenny Hirst

IDDT welcomes the submission of letters and editorial articles for consideration of publication in future issues of the IDDT Newsletter. The editor and trustees do not necessarily endorse any opinions or content expressed by contributors and reserve the right to refuse, alter or edit any submission before publication. No part of this publication may be reproduced in any form without the prior written permission of the editor.

**Insulin Dependent Diabetes Trust**
PO Box 294
Northampton
NN1 4XS

tel: 01604 622837
fax: 01604 622838
e-mail: support@iddtinternational.org
website: www.iddtinternational.org