Insulin – A Voice for Choice
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**Jenny Hirst**
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9 figures and 8 tables, 2007

Arthur Teuscher
On October 29, 1982, the United States Food and Drug Administration (FDA) approved an application by Eli Lilly and Company of Indianapolis, Ind. to market its new synthesized recombinant DNA insulin. The FDA’s 4-month review of this first medical product of biotechnology was remarkably less than the average time for drug reviews in those days, suggesting unusual enthusiasm by the FDA staff for the product. The product’s name, also subject to FDA approval, was ‘Humulin’, a name which contradicted the agency’s long-standing regulation disallowing “fanciful” names or false and/or misleading claims embedded in the name’ [1]1.

In fact, and as noted in this remarkable book, Humulin and other synthetic insulins marketed by other companies are by no means identical to natural human insulin as the name, and the marketing, have suggested. Nevertheless, manufacturers re-enforced this misapprehension with a sophisticated and aggressive marketing strategy based, in part, on the premise that ‘human’ insulin is identical to insulin produced by nondiabetics and therefore must be safer and more effective than insulin obtained from animals. Thousands of physicians, targeted by drug company sales representatives, have internalized that message and have repeated it to their patients.

1 An example of an intervention by the FDA was its ruling that an oral contraceptive marketed as ‘Marvelon’ in many countries could not carry this name in the United States since it suggested that the drug was ‘marvelous’. Similarly, ‘Humulin’ suggests that the product is human insulin, a false claim.
It would take a courageous and innovative person to challenge the claims of such a well-financed pharmaceutical marketing strategy. However, as this book demonstrates, Professor Arthur Teuscher was not only well qualified to take on the task but also had the drive and social responsibility to devote an enormous amount of time and energy to this issue. After graduating from the University of Bern Medical School in 1951, he pursued postgraduate studies in endocrinology at the Medical Academy of the Free University of Berlin and the Heinrich-Heine University of Düsseldorf, in nephrology at the University of Bern, and in diabetology at the Joslin Clinic in Boston, Mass. He returned to Bern to specialize in diabetes and other endocrine diseases, becoming one of the first diabetologists in Europe. In 1966 Professor Teuscher established the Diabetes Section at the University of Bern Medical School and in time was appointed Professor of Diabetology. He founded the European Diabetes Epidemiology Group and the European Diabetes and Nutrition Study Group and became a respected member of the World Health Organization’s Multinational Study Group on Vascular Diseases in Diabetes.

Like many physicians, Professor Teuscher was influenced by the persistent promotion of ‘human’ insulin as a significant breakthrough in diabetes treatment. Hoping and expecting to pass the benefits of science and technology to his diabetic patients he suggested that some of them switch to the new product soon after it became available. He did this in good conscience, persuaded, in part, by the scientific enthusiasm worldwide for this first example of the application of recombinant technology to medicine.2

As poignantly described in the chapter on Hazards of ‘Human’ Insulin Hypoglycemia, Professor Teuscher was deeply affected by the death of one of his patients who had chosen to switch to ‘human’ insulin. Until his death, this 20-year-old man had controlled his diabetes very intelligently. Indeed, he was a pharmacology graduate student and certainly had a good understanding of his disease and insulin treatment. This tragedy motivated Professor Teuscher to begin on his extraordinary and resolute campaign to alert physicians and patients to the potential dangers of synthetic insulin and to his tireless efforts for the continued availability of natural insulin.

His first notable achievement in this endeavor was to co-author, with W.G. Berger, an article in The Lancet documenting the case history of this patient and of two others who experienced life-threatening problems with ‘human’ insulin. The study found that, after a switch from animal to ‘human’ insulin, hypoglycemia symptoms in all three patients were less pronounced, resulting in diminished

2 It may be that this enthusiasm accounts for the remarkably rapid approval of the product by the US Food and Drug Administration (FDA) in October 1982.
warnings of impending unconsciousness [2]. The article marked the beginning of a long crusade to develop an evidence-based approach to insulin therapy which underscored the importance of safety and efficacy, as well as patients’ quality of life. Soon after Professor Teuscher and Dr. Matthias Egger published a more comprehensive study of the problem in The Lancet entitled Human Insulin Hypoglycaemia Unawareness, effectively challenging the safety of ‘human’ insulins in some diabetics. As noted elsewhere in this book, this was followed by a series of scientific articles in other major medical journals which established without doubt that ‘human’ insulin is indeed less safe than natural insulin in some diabetics.

Professor Teuscher focused much of his efforts on both insulin producers and physicians, but he also did what very few diabetologists had done: he shared his evidence with the emerging movement of diabetic patients fighting for continued access to animal insulin. Despite the acknowledgment by the manufacturers of the potential dangers of ‘human’ insulin – as evidenced by the boxed drug warning included on all ‘human’ insulin labels – they promptly started to withdraw natural insulin from markets all over the world in favor of more expensive ‘human’ brands. As a result, the profits of insulin manufacturers increased significantly, as more affordable animal insulins disappeared from the market in many countries around the world. An unethical and insidious marketing ploy left many local pharmacies without animal insulin, forcing diabetic patients to buy ‘human’ insulin. This effectively forced a switch, often without the informed consent of the patient, and with little or no information about potential side effects.

It is disturbing to note that market forces have been particularly heavy-handed in developing countries with the result that animal insulin, whether imported or domestically produced, is impossible to obtain in many cases. In response, the persistent and ever-innovative Professor Teuscher extended his reach by bringing animal insulin from India to Dar es Salaam in Tanzania in a remarkable self-sustained program developed with the local City Council Urban Health Project and the Swiss Tropical Institute and supported by the Foundation on Nutrition and Diabetes in Bern.

It is difficult to contest the might of ‘Big Pharma’, but fortunately advocates of animal insulin are also very much involved, as described by Jenny Hirst in the chapter on Advocacy. Professor Teuscher has earned international respect

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3 Dr Egger is currently Chair, Clinical Reader in Epidemiology and Public Health Medicine, Department of Social Medicine, University of Bristol, UK.

4 This is also the case in the United States, where pork and beef insulins have been completely withdrawn from the market. However, patients may import small amounts of natural insulin for their personal use.
and admiration within what is now an emerging global movement to support an animal insulin option. Like him, activists are working to ensure that scientific evidence continues to influence the treatment and management of this complex disease. Animal insulin is experiencing a resurgence in the UK and in Canada, and with ongoing efforts at both national and international levels, there is good reason to hope that this will occur in other countries as well.

We are certain that as others join Professor Teuscher and the advocates identified in this book, ‘the right of free choice’ will be secured, and natural insulin will become available and affordable worldwide for all who need it.

Philip Corfman

References

Prologue

Dissimilarity of Natural and Recombinant ‘Human’ Insulin

Case History of M.B.
This is the unique history of 61-year-old M.B., a Swiss woman with type 1 diabetes, who grew up on a farm in the canton of Bern after World War 2. She developed juvenile diabetes at the age of 5 and presented with unstable diabetes from youth onwards.

From Porcine to ‘Human’ Insulin with Hypoglycemia Unawareness
In 1987 a diabetologist changed her regimen, replacing porcine with DNA recombinant ‘human’ fast-acting and isophane insulin. Her diabetes control deteriorated immediately. She had at least one or two unconscious hypoglycemia events per week. Her diabetologist went so far as to suggest that she, being a religious person, should pray and ‘leave her life in the hands of God’ in order to obtain a more stable diabetes.

Unconscious Hypoglycemia Unawareness in West Africa
M.B. took the doctor’s advice seriously and moved to Conakry (Guinea) in 1987 with her husband. They set up a health center and a school in the outskirts of the capital, both of which are still operating. She continued to suffer abrupt hypoglycemia events, without any warning symptoms, 2–3 times a week, occasionally twice a day, and ongoing mental depression. She would drop unexpectedly to the floor. Her husband had to reanimate her with glucose and force her to eat when he came home from work.
‘Human’ Insulin Was Not the Solution: Returning to Switzerland

M.B. was referred to the diabetes center in Bern by a friend whose diabetic son was back in good health after changing from ‘human’ back to porcine insulin. He had had several car accidents due to hypoglycemia unawareness while on ‘human’ insulin, but, once on porcine insulin, he no longer had any accidents, and was able to get his driving license back.

M.B. came under my care in 1995. An African physician had recommended that she returned to Europe because of her continuing unconscious hypoglycemic events, often ending in collapse and sometimes with epileptic seizures.

Going back to ‘Friendly’ Porcine Insulin

At her first visit, she was on 3–5 units of fast-acting ‘human’ insulin before meals, 8–10 units of isophane ‘human’ insulin at breakfast and 2–3 units in the evening. Her HbA1c was 8%. At the first consultation, she was switched to fast-acting and isophane porcine insulins, the same insulin types, with the same doses. She immediately stopped being depressed and emotionally unstable, and she regained the classical hypoglycemia warning symptoms of sweating, tremor, and hunger. This continued to be the case for the next 7 years.

Her blood sugar values were still unstable, but without abrupt hypoglycemia coma. Changing from 10 units of porcine isophane insulin to 3 units of porcine Semilente MC (amorphous zinc suspension) at bedtime prevented postmidnight hypoglycemia. The kinetics and dynamics of porcine insulin Semilente MC in small doses at bedtime (10-12 p.m.) very rarely produce post-midnight hypoglycemia.

A trial for smoother control using an insulin pump was not successful.

Islet Cell Transplantation: Pancreatic Human Insulin Is Not Identical to Recombinant ‘Human’ Insulin

M.B. was selected as one of the first Swiss candidates for an intrahepatic islet cell transplantation under the Edmonton Protocol at the University Hospital of Geneva. The intrahepatic injection of islet cells from two human pancreases was performed in 2002.

For the last 5 years, the patient has had no insulin treatment. She occasionally takes 1 unit of porcine fast-acting insulin ‘as a precaution’ at her own discretion when her blood sugar is 8 mmol/l after a bit of chocolate. Her HbA1c dropped from 8% before the transplantation to 5.5–5.9% (normal) and has remained at that level for the last 5 years. Islet transplantation resulted in stabilized blood glucose levels of 4–6 mmol/l before breakfast and rarely 7 before the evening meal.

5 See http://www.islet.ca/.
The main subjective features of a full quality of life have been restored after transplantation: happiness, clear voice, involvement in physical and mental work, disappearance of depression, and the ability to continue with her health project in Guinea. She tolerates immunotherapy well. Laboratory data show absence of diabetes with normal glucose tolerance and no evidence of long-term neurovascular or renal disease.

**Conclusion**

M.B. is a case of successful islet cell transplantation, but I maintain that in many cases of ‘human insulin hypoglycemia unawareness’, a transplantation can be prevented by changing from synthetic ‘human’ to porcine insulin.

In M.B.’s case, full quality of life could only be obtained with islet cell transplantation.