

# From Injection to Ingestion: 100 Years of Diabetes

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These are exciting times for physicians dealing with endocrinology, diabetes, and metabolic disorders. The newer developments have engulfed all areas and have sparked renewed interest in research at both the molecular and clinical levels.

## What have we learned about diabetes?

Even up until just 100 years ago, not much was done about diabetes, particularly in the realm of therapeutics. However, at that time some startling advances in medicine were made, such as the discovery of bacteria as pathogenic, the importance of anti-sepsis, the development of anesthesia and vaccinations, and the description of diabetes was refined (what we now call Type 1 and Type 2). The age of scientifically proven therapeutics and evidence-based medicine had simply not arrived.

In 1869, Paul Langerhans described

islets of Langerhans in the pancreas. In 1920, great Canadian scientists Frederick Banting and Charles Best made history with a Nobel prize when they discovered insulin. As it turned out, the first child to receive insulin, Leonard Thompson, lived 13 years longer (thanks to the insulin), before dying of bronchopneumonia.

The addition of new sulphonylureas, thiazolidinediones, and meglitinides to the oral armamentarium against hyperglycemia has helped

Table 1

### Benefits of insulin analogs

- Better pharmacodynamics
- Flexibility
- Cost-effective
- Convenient to use
- Peakless, 24-hour action (especially glargine)
- Overall improved glycemic control
- Less incidence of hypoglycemic reactions

many patients. More recently, important advances, including the refinement of insulin pumps and regimens for continuous, subcutaneous insulin infusion have offered new hope to physicians and patients. Deoxyribonucleic acid (DNA) recombinant technology has led to the ability to synthesize insulin analogs (short-acting insulin lispro and aspartate, and long-acting insulin glargine), which have many added benefits (Table 1).

Recent technologic advances have also made it feasible to deliver insulin to the alveolar space by inhalation. Insulin is delivered either in a fine-powdered or in a liquid aerosol formulation. Numerous Phase II clinical trials have demonstrated the effectiveness, safety, and acceptability of inhaled insulin in both Type 1 and Type 2 diabetes.

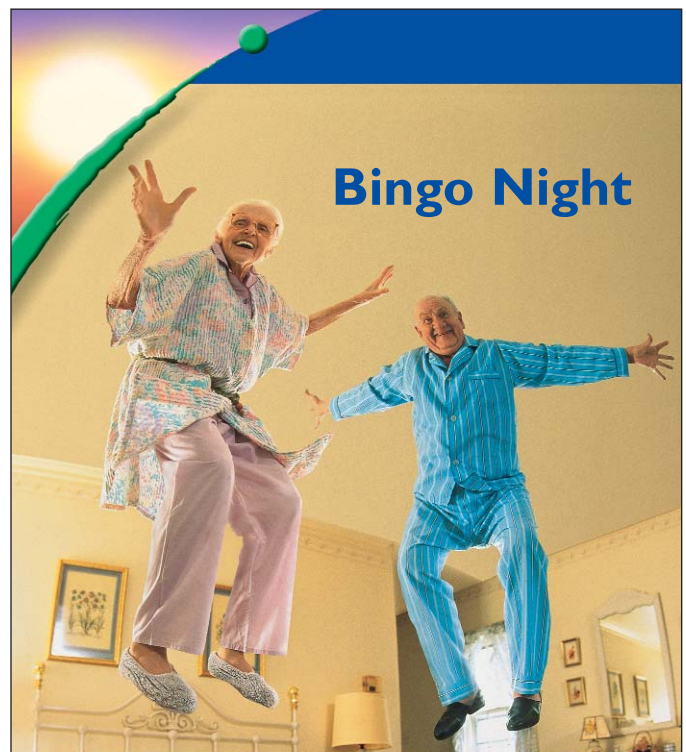
Amylin, a second  $\beta$ -cell hormone, co-secreted with insulin, complements the effects of insulin in post-prandial glucose control. An amylin deficiency in patients with advanced  $\beta$ -cell failure can be corrected using the amylin analog pramlintide as an adjunctive therapy to insulin. This treatment has been shown to improve post-prandial and overall glycemic control without increasing the risk of hypoglycemia or weight gain. Non-invasive glucose monitoring with GlucoWatch<sup>®</sup> and Continuous Glucose Monitoring System<sup>®</sup> has also opened new frontiers.

Another diabetes research benchmark again came from a dedicated Canadian team, performing islet-cell transplantation done by Edmonton protocol. The team successfully achieved complete metabolic independence from insulin in seven peo-

ple with Type 1 diabetes. Not only did therapeutics see a high tide, but the diabetes prevention techniques (including the landmark Diabetes Prevention Program trial) again proved the common wisdom of lifestyle modification in glucose-impaired individuals. Other pharmacologic approaches using troglitazone and metformin show promising results in diabetes prevention trials.

Two new anti-obesity medications (sibutramine and orlistat) were embraced with open arms by physicians and patients after withdrawal of the much controversial fenfluramine and the inability of

*Two new medications, sibutramine and orlistat have shown desirable effects when combined with lifestyle modifications.*



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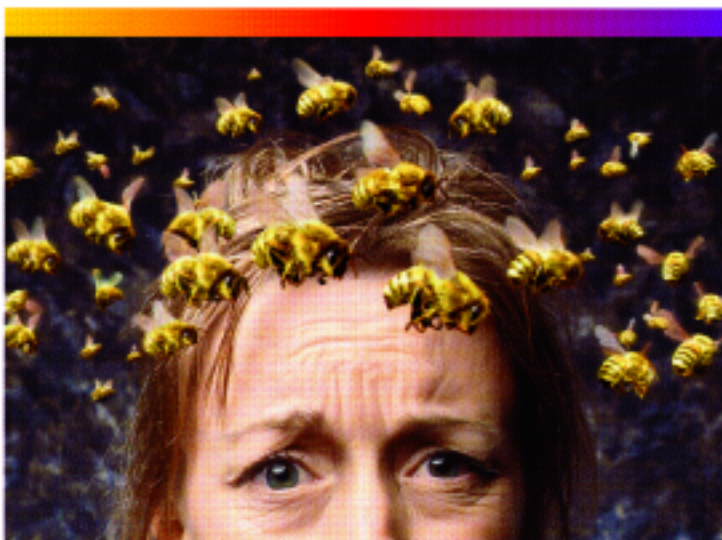
amphetamines to be used for the long term. Sibutramine and orlistat have shown desirable effects in long-term use when coupled with lifestyle modifications.

The recent era of bone and metabolism research saw the advent of anabolic therapy with parathyroid hormone, as well as the evolution of newer, better tolerated, and effective oral bisphosphonates (alendronate and risedronate). Recently, the National Institutes of Health agreed on new consensus guidelines for the treatment of primary hyperparathyroidism. In recent trials, two oral agents, alendronate and raloxifene, were employed for the first time for medical instead of surgical treatment of the milder form of primary hyperparathyroidism. These agents showed promising results.

A new agent, ezetimibe, was recently launched in Canada to treat hypercholesterolemia. Ezetimibe works by selectively inhibiting the uptake of cholesterol from the intestinal lumen at the level of the enterocyte in the intestinal brush border while having no effect on other sterols or lipid-soluble vitamins. The treatment has demonstrated marked improvement in low-density lipoprotein cholesterol if co-administered with statin therapy.

### Still a lot to learn

Having said all this, I must add that although we have come a long way, there still needs to be much done. There is no doubt the most dramatic, definitive discoveries have yet to be made. 



## ANXIOUS TO FIND OUT MORE?

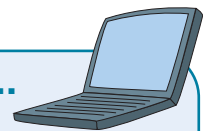
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