Insulins

New advances promise tighter control with less hypoglycemia

BY STUART H. KREISMAN, MD AND ADAM S. WHITE, MD

The discovery of insulin by Banting and Best in 1921 represented a cardinal moment in the history of medicine and a life-saving one for thousands of patients with type 1 diabetes mellitus. It's now understood that there's a clear relationship between optimal glycemic control and the prevention of diabetic complications. Years of research have seen the development of many types of insulin, with different chemical structures, mechanisms of delivery, and action profiles. Insulin has become an easier, and more adaptable, choice for the management of both type 1 and type 2 diabetes.

Stuart H. Kreisman, MD, is a clinical assistant professor at the University of British Columbia (UBC) in the Division of Endocrinology and Metabolism. He is also on staff at St. Paul's Hospital in Vancouver.
Adam S. White, MD, is completing his endocrinology fellowship at UBC.

Insulin comparisons

Insulin preparation	Onset of action	Peak of action (hrs)	Duration (hrs)
Short-acting			
regular	30-60 min	2-4	6-8
aspart, lispro	5-15 min	1-2	3-4
Intermediate-acting			
NPH	1-3 hrs	5-7	13-16
Long-acting			
glargine	1-2 hrs	no real peak	24
detemir	1-2 hrs	no real peak	up to 24

Special considerations

- driving — by law, patients must test blood sugars before driving and every 4 hours on long trips
- emergency kit — crucial delivery of glucose in both conscious and unconscious conditions, e.g. glucagon
- MedicAlert bracelet — for all
- weight gain — common; tight blood sugar control is more important
- skin changes at injection sites
  - occasional bruising
  - lipohypertrophy — at overused site, alters insulin absorption
  - best practice is to rotate sites

Short-acting

Regular human insulin

- remains in widespread use
- inexpensive but inflexible
- 15-30 minutes before a meal
- hypoglycemia risk if meal is delayed
- peaks later (3-4 hrs) than glucose following a meal (1-2 hrs)
- risk of low blood sugar necessitates snacks

Ultra-fast-acting

- aspart (NovoRapid), lispro (Humalog), glulisine (Apidra, not yet available in Canada)
- rDNA origin
- direct injection or by insulin pump
- less hypoglycemia than regular
- similar to response of normal pancreas to ingestion of food
- injected when food is ready
- may be given after a meal
- useful when final intake is uncertain, on sick days, or for young children

Long-acting

Intermediate duration

- neutral protamine Hagedorn (NPH)
  - today's standard long-acting insulin
  - peak effect ~6 hours
  - generally lasts ~12 hrs
  - onset of action 1-3 hrs
  - usually needs twice daily injection
  - not a good basal insulin — prominent peak, leading to risk of low blood sugar, most importantly in the middle of the night
  - this can be lessened by moving evening injection to bedtime

Longer-lasting

- insulin detemir (Levemir) and glargine (Lantus)
  - rDNA origin
  - theoretical advantage of a peakless insulin profile
  - don't mix or use in same syringe as other insulins
  - can be administered once daily, either morning or bedtime
  - on occasion, twice daily injections are needed, especially for type 1 diabetics on detemir
  - twice daily dosing produces flatter profile curves
  - fewer symptomatic and nocturnal hypoglycemic episodes than NPH
  - HbA1c reductions similar to NPH
  - detemir
    - less day-to-day variability
    - may be more weight-neutral than others
    - allergic reactions reported
  - glargine
    - increased affinity for insulin-like growth factor 1 (IGF-1) receptors
    - whether this affects diabetic retinopathy is being investigated in post-marketing studies
- lente, ultralente, beef and pork insulins
  - no longer readily available
  - obtainable in special circumstances

Insulin regimens

Pre-mixed insulin

- various ratios of short- and long-acting insulins, e.g. 30/70
- given twice daily
- many different preparations available
- ease of administration, but no flexibility for adjustments
- not appropriate for those interested in standard of care therapy
- despite theoretical shortcomings, they remain a top-seller

Split-mixed

- separate injections of short- and long-acting, at breakfast and dinner
- greater amount of flexibility
- adjust components separately

Basal-bolus/multiple daily injections (MDI)

- 3 or 4 injections/day
- recommended standard of care
- 1-2 injections of long-acting insulin plus short-acting insulin bolus at each meal and possibly snacks
- combinations of ultra-fast with long-acting analogues are best
- patients can learn to "carb-count," adjusting insulin to anticipated food amounts

Insulin pump

- continuous subcutaneous insulin infusion (CSII)
- provides flat or adjustable basal insulin via ultra-fast-acting analogue with additional boluses for meals and snacks
- requires dedication to care, not simply "plug and play"
- slightly lower HbA1c levels than MDI in meta-analysis
- many individuals experience less hypoglycemia
- newer models incorporate continuous glucose monitoring

Inhaled insulin

- available in USA (Exubera), shortly in Canada
- new short-acting insulin delivery
- cumbersome hardware
- long-term effects on respiratory function unknown, pulmonary function tests recommended
- contraindicated in smokers

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