Continuous glucose monitors (CGMs) measure interstitial fluid (ISF) glucose, and provide information about continuous glucose fluctuations that is not otherwise captured by intermittent blood glucose testing. CGMs may benefit patients having difficulty controlling their blood sugar or during initiation or monitoring of insulin pump use. CGMs require calibration with finger-stick tests and supplement, but do not replace conventional blood glucose testing. CGM values correspond to blood glucose values taken approximately 13-18 minutes earlier and may differ from metered readings.

The Technology

Continuous glucose monitors (CGMs) measure glucose levels in the interstitial fluid surrounding skin cells, providing continuous information about glucose fluctuations that is not otherwise captured by intermittent testing. These devices require calibration with blood glucose levels as determined by finger-stick tests. Errors of 20% or more have been noted in blood glucose metered readings. This error could be transferred to CGMs during calibration and thereby affect their overall accuracy. CGMs can record when meals, insulin injections, hypoglycaemic episodes and exercise occur.

The Continuous Glucose Monitoring System (CGMS) (MiniMed Inc; Sylmar, CA, USA) supplements finger-stick glucose measurements by monitoring glucose fluctuations over a 72-hour period. A needle sensor is inserted under the patient's abdominal skin and is wired to an externally worn monitor. Glucose in the interstitial fluid reacts with glucose oxidase on the needle, producing hydrogen peroxide. This chemical reaction generates measurable current. Glucose is measured over a range of 2.2 - 22.2 mmol/L. Readings, taken every 10 seconds, are averaged every five minutes and stored in the monitor's memory. Averaged readings are transferred to a computer for therapeutic planning by a physician; no real-time measurements are provided directly to the patient.

The GlucoWatch Biographer system (Cygnus Inc; Redwood City, CA, USA) is worn like a wristwatch for up to 12 hours at a time. An AutoSensor containing glucose oxidase-laden gel discs and electrodes snaps onto the back of the device. When a low electric current passes between the electrodes, glucose is extracted through the intact skin by electro-osmotic flow. ISF glucose collects in the discs and reacts with glucose oxidase producing hydrogen peroxide. The electrodes measure this reaction every 20 minutes.

Regulatory Status

<table>
<thead>
<tr>
<th>Device</th>
<th>Country</th>
<th>Approval</th>
<th>Status</th>
</tr>
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<tbody>
<tr>
<td>MiniMed</td>
<td>US</td>
<td>June 1999</td>
<td>Supplement conventional testing</td>
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<tr>
<td>CGMS</td>
<td>Canada</td>
<td>May 2000</td>
<td>Class III device licence</td>
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<tr>
<td></td>
<td>Europe</td>
<td>June 2000</td>
<td>Available by prescription</td>
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<tr>
<td>GlucoWatch</td>
<td>Europe</td>
<td>Dec 1999</td>
<td>Approved</td>
</tr>
<tr>
<td>Biographer</td>
<td>US</td>
<td>March 2001</td>
<td>Supplement conventional testing</td>
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<tr>
<td></td>
<td>Canada</td>
<td></td>
<td>Not approved as of 05/06/02</td>
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</table>

Patient Group

Diabetes mellitus (DM) is a chronic condition wherein the body is unable to produce or use insulin. Without insulin regulation, cells cannot absorb sufficient glucose from the bloodstream or derive energy from food, resulting in high blood glucose levels. Long-term high blood glucose values are associated with damage to the eyes, kidneys, nerves and large blood vessels. Diabetes is the leading cause of blindness, kidney failure, and lower leg amputation and is also a major cause of premature heart disease and other vascular diseases.
There are two types of DM, type 1 and type 2. Accounting for 10% of cases, type 1 occurs when islet cells of the pancreas do not produce insulin. With its onset, typically in the teen or young adult years, type 1 DM requires daily insulin injections. Approximately 90% of cases are type 2, resulting from insulin resistance and partial deficiency. Typically affecting people over 40 years of age, type 2 DM can sometimes be controlled by diet alone, however, medications may be required. Over two million people have DM and it is the seventh leading cause of death in Canada.

CGMs provide information about glucose fluctuations that may be of particular benefit to patients with type 1 DM that is difficult to control. This includes patients with asymptomatic hypoglycemia, nocturnal hypoglycemia, unpredictable blood glucose levels regardless of therapeutic adjustments, and patients starting or changing insulin regimens.

**Current Practice**

Maintaining blood glucose at near-normal levels reduces the risk of long-term complications. However, tight control of glucose levels increases the risk of low blood glucose levels that are associated with significant consequences. Periodic testing for glycosylated hemoglobin (HbA1c) is recommended; this assesses the average blood glucose levels over the preceding three months.

Self-monitoring allows persons with diabetes to measure their blood glucose levels at home and adjust therapy appropriately. Self-monitoring requires a finger-prick to draw blood several times a day. Alternative site testing on an arm or leg may reduce callus formation and loss of sensation from frequent testing. Many patients are reluctant to perform finger-stick tests frequently due to inconvenience, pain, and expense, making it difficult to adjust therapy appropriately. Glucose meter types differ by: the amount of blood required, testing time, size of the meter and presentation of the memory data.

**Administration and Cost**

Neither the CGMS device, the sensors, nor the procedure for insertion are covered by Canadian provincial health insurance plans (Mark Mailloux, MiniMed, Ile des Soeurs, PQ: personal communication, 2002 May 7).

**Rate of Technology Diffusion**

Available by prescription only, the CGMS supplements standard glucose measurement in specific situations. Glucose fluctuations identified with the CGMS can determine more precisely when finger-stick tests should be done. Therapy can then be adjusted to compensate for glucose fluctuations. Current studies are investigating CGMS use in paediatric and non-Caucasian patients, and patients with type 2 DM, concomitant disease states, or gestational diabetes.

The GlucoWatch is used as an adjunct to standard testing by patients at home and in health care facilities. Cygnus received supplemental pre-market approval from the FDA for the GlucoWatch G2 Biographer. This technology has a shorter warm-up time, and displays and stores more readings than the first-generation GlucoWatch.

**Concurrent Developments**

Several biosensors are under development; from a wireless system by TheraSense, to a transdermal patch that draws ISF glucose for reading by a handheld meter (Technical Chemicals and Products Inc.). Bioject Medical Technologies is designing a combined patch and sensor that produces a continuous reading. The Diasensor 2000 monitor (Biocontrol Technology Inc, Pittsburgh, USA), based on infrared technology, is used in Europe but is not yet available in North America.

**The Evidence**

**CGMS:**
Evidence of CGMS use, primarily in type 1 DM, includes a randomized controlled trial (n=11), several prospective comparative studies (n=250), and a post market surveillance trial (n=238). CGMS measurements correlate closely...
The Canadian Coordinating Office for Health Technology Assessment (CCOHTA) is a non-profit organization funded by the federal, provincial and territorial governments. (www.ccohta.ca)


15. TheraSense continuous glucose monitor R&D to get boost from IPO. The Gray Sheet 2001;27(29).


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