PRODUCT SHEET

Metabolon

Quantose® IGT

Disease Summary

Impaired Glucose Tolerance

Impaired Glucose Tolerance is a prediabetic state of hyperglycemia that is associated with insulin resistance and an increased risk of cardiovascular pathology (Barr, 2007). The condition occurs when blood glucose levels remain high for an extended period after oral ingestion of glucose but not high enough to be diagnosed as type 2 diabetes. Historically Impaired Glucose Tolerance has been diagnosed via the oral glucose tolerance test (OGTT) with 2-hour plasma glucose (2hPG) values of 140-199 mg/dL. "However, its complexity, poor reproducibility, associated costs, time requirement and patient inconvenience often inhibit routine use in clinical practice. The OGTT is rarely performed for purposes other than clinical research and to assess glycemia status in women during pregnancy" (Rich 2013).

Impaired Glucose Tolerance is associated with obesity, dyslipidemia (high triglycerides and/or low HDL cholesterol), and hypertension (Nathan, 2007). Persons with Impaired Glucose Tolerance have in increased risk of developing type 2 diabetes and cardiovascular disease. (DeFronzo, 2011).

Test Summary

Quantose® IGT

Quantose® IGT identifies Impaired Glucose Tolerance with a single fasted blood draw by measuring a panel of biomarkers comprised of two small organic acids (α-hydroxybutyric acid (AHB) and 4- methyl-2-oxopentanoic acid (4MOP)), 2 lipids (oleic acid and linoleoylglycerophosphocholine (LGPC)), a ketone body (β-hydroxybutyric acid (BHBA)), an amino acid (serine), a vitamin (pantothenic acid (vitamin B5)), and glucose. The Quantose® IGT algorithm was developed using fasting samples taken from subjects just prior (time=0) to undergoing an OGTT in the RISC (Relationship between Insulin Resistance and Cardiovascular disease) study 3 year follow up (Cobb, 2015). This study was a prospective, observational, cohort study in clinically healthy people at baseline between the ages of 30 and 60 years recruited from 13 European countries (Hills, 2004). Fasting samples from 843 normal glucose tolerant (NGT) and 112 IGT subjects taken at the RISC 3 year follow up were utilized in the algorithm development.

The Impaired Glucose Tolerance cut-off of 60 was defined by the top tertile of scores from the RISC study. Concentrations of the panel biomarkers are measured by clinical chemistry (glucose) and mass spectrometry (UHPLC-MS/MS) based quantitation and then combined to generate the Quantose® IGT Score.

The Quantose® IGT Score is based on a logistic regression algorithm utilizing the quantitative measures of AHB, oleic acid, LGPC, BHBA, 4MOP, serine, vitamin B5 and glucose and was designed to estimate the probability of being IGT. Fasting plasma levels of AHB, oleic acid, LGPC, BHBA, 4MOP, serine, vitamin B5 and glucose individually correlate significantly with the 2hPG value from the OGTT. The algorithm score is then converted to the Quantose® IGT score having a range of 1-200 by an arithmetic calculation where higher scores denote higher risk of having Impaired Glucose Tolerance.

Clinical Use

- To identify patients with Impaired Glucose Tolerance (IGT)
- Guide treatment strategy for patients with Impaired Glucose Tolerance

This Guide provides information relating to the selection, utilization, and interpretation of the Quantose® IGT test. Information provided is based on peer-reviewed publications and clinical practice guidelines.

Individuals Suitable for Quantose®IGT Testing

Adults who are overweight (BMI ≥25kg/m2 or ≥23kg/m2 in Asian Americans) and have one or more of the following risk factors:

- Physical inactivity
- Hypertension (≥140/90 mmHg or on therapy for hypertension)
- HDL cholesterol level < 35mg/dL (0.90 mmol/L) and/or a triglyceride level > 250 mg/dL (2.82 mmol/L)
- High risk ethnic background (e.g., African American, Latino, Native American, Asian American, Pacific Islander)
- First-degree relative with diabetes
- Delivered a baby weighing > 9 lb. or diagnosed with gestational diabetes mellitus
- Polycystic ovary syndrome
- Other clinical conditions associated with Insulin Resistance (e.g., severe obesity, acanthosis nigricans)

Fasted 8-10 hours

Method

Liquid chromatography, tandem mass spectrometry (LC-MS/MS) using the stable isotope dilution technique to quantify AHB, LGPC, oleic acid, BHBA, 4MOP, serine and vitamin B5 (µg/mL)

- EDTA plasma samples are extracted with methanol and spiked with stable isotope labeled standards of AHB, LGPC, oleic acid, BHBA, 4MOP, serine, and vitamin B5
- Separation via ultra-high-performance liquid chromatography (UHPLC)
- Detection and quantitation via tandem mass spectrometry

Plasma glucose is quantified (mg/dL) using the Abbott glucose assay on the Architect platform

Analyte concentrations used in conjunction with an algorithm to estimate probability of being IGT.

Report includes concentrations of AHB, LGPC, oleic acid, BHBA, 4MOP, serine, vitamin B5 and glucose along with the Quantose®IGT score.

Interpretive Information

It is recommended that the Quantose®IGT test be administered to patients with relatively stable weight (+/- 3 lbs. over one month) and before and after diet and exercise programs.

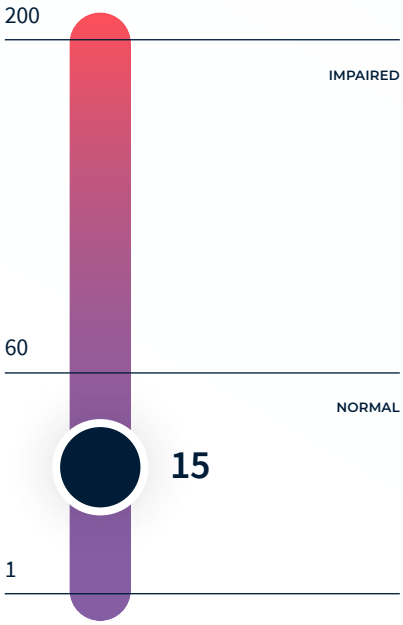
In a 12-week, 70 subject study, the Quantose®IGT measurement demonstrated fluctuations in individual analytes in subjects experiencing active weight loss. Further study is required to more fully understand potential correlations between active weight loss and the Quantose®IGT measurement. In a situation when a patient is experiencing active weight loss, clinicians should interpret the Quantose®IGT test results with caution (Metabolon data on file).

Test Scores

	REFERENCE INTERVALS		
AHB	1.92 - 7.37 µg/mL	**Oleic acid**	25.9 - 114 µg/mL
LGPC	7.60 - 25.4 µg/mL	**BHBA***	1.40 - 38.8 µg/mL
4MOP	2.60 - 6.20 µg/mL	**Serine**	7.10 - 14.8 µg/mL
Vitamin B5	0.265 - 0.150 µg/mL	**Glucose**	**

*The BHBA (beta-hydroxybutyrate) assay in Quantose®IGT has not been validated for the diagnosis of diabetic ketoacidosis. If this condition is suspected, other definitive testing may be considered.

**Normal = <100 mg/dL; Prediabetic = 100-125 mg/dL Diabetic= ≥126 mg/dL(ADA 2015)



Patients with a Quantose®IGT Score of 60 or higher are indicative of having impaired glucose tolerance. This cut-off is defined by the top tertile of scores from a study of 955 clinically healthy, non-diabetic people recruited from 13 European countries having a 12% prevalence of IGT (Cobb, 2015). Quantose®IGT test score reference intervals were established using 456 non-diabetic subjects at risk for diabetes (IFG, IGT, and/or FINDRISC score > 12).

Performance

Quantose®IGT scores have an AUC of 0.82 for the ROC curve for the identification of people with Impaired Glucose Tolerance using the top tertile cut-off of >60. Using this same criterion, the test has a sensitivity of 78% and a specificity of 72%. These data were generated in the 955 RISC study subjects. (Cobb, 2015)

Specimen Requirements and Shipping/Handling

- 0.5 mL refrigerated or frozen plasma (EDTA (K2)/lavender top tube).
- Patient must be fasted for 8 to 10 hours prior to sample collection
- Refrigerated samples should be sent overnight with cold packs to maintain 4°C
  Frozen samples should be sent on dry ice and remain frozen at -20°C to -80°C

Caution: It is critical that plasma is separated from whole blood within 1 hour of collection to ensure integrity of results.

REFERENCE INTERVALS

STORAGE TEMP.	SPECIMEN TYPE	COLLECTION VIAL	TRANSPORT VIAL	MINIMUM VOLUME	SHIPMENT CONDITION	STABILITY
Refrigerated 4°C	Plasma	EDTA (K2) / Lavender Top	Thermo Scientific™ Nalgene™ Cryogenic Tube P/N 5000 0050	0.5 mL	Cold Pack / Overnight	96 hours
Frozen -20°C-80°C	Plasma	EDTA (K2) / Lavender Top	Thermo Scientific™ Nalgene™ Cryogenic Tube P/N 5000 0050	0.5 mL	Dry Ice / Overnight	5 months

Note: Detailed shipping and handling information guidance available upon request.

References

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info@metabolon.com

+1 (919) 572-1711
info@metabolon.com
www.metabolon.com

617 Davis Drive, Suite 100, Morrisville, NC, 27560

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