Tracer Experiments with Glucose

Fig. 1 Glucose homeostasis.

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**Purpose**
This publication will describe the technical details of using stable isotope tracers to determine glucose flux, recycling, oxidation, and synthesis rate from gluconeogenic precursors.

**Introduction**
The primed constant infusion of stable isotope labeled glucose has been extensively validated as a reliable approach to quantifying glucose kinetics. This approach can be used to explore whole body glucose homeostasis under various perturbations such as exogenous infusions of glucose and insulin. Sensitive methods for measuring labeled glucose in plasma have been developed to permit quantitation with 50 - 100 µl of plasma. Thus, these studies can be performed even in newborns.

**Glucose Flux**
Determines the whole body flux rate of glucose. If the amount of glucose intake is known, the glucose production rate can be calculated.

**Protocol**
- **Best Tracer:** 6,6-D2-Glucose
- **Priming Bolus Dose:** 14.0 µmol/kg
- **Infusion Pump Speed:** 0.174 cc/min
- **Infusion Rate:** 11.5 µmol/kg/hr
- **Infusion Time:** 140 min.
- **Sampling Times:** 0, 90, 100, 110, 120 min. (Plasma)
- **Diet Protocol:** Fasted or Fed
- **References:** Bier et al., Diabetes 26, 1005-1015, 1977  
  Bier et al., Diabetes 26, 1016-1023, 1977  
  Shaw and Wolfe, Surgery 97, 557-568, 1985

**Glucose Recycling**
Determines glucose and fructose recycling rates in addition to glucose flux and production rate. The measured rates of cycling in glycolysis and gluconeogenesis represents the total substrate cycling rates between glucose and glucose-6-phosphate and fructose-6-phosphate and fructose-1,6-diphosphate.

**Protocol**
- **Best Tracers:** 6,6-D2-Glucose and 2-D1-Glucose
- **Priming Bolus Dose:** 17.8 µmol/kg each tracer
- **Infusion Pump Speed:** 0.174 cc/min
- **Infusion Rate:** 13.2 µmol/kg/hr
- **Infusion Time:** 140 min.
- **Sampling Times:** 0, 90, 100, 110, 120, 130, 140 min. (Plasma)
- **Diet Protocol:** Fasted or Fed
- **References:** Shulman et al., J. Clin. Invest. 76, 757-764, 1985  
  Miyoshi et al., J. Clin. Invest. 81, 1545-1555, 1988
**Glucose Oxidation**
The rate of glucose oxidation can be calculated using a $^{13}$C-labeled glucose tracer. Samples of blood are collected to determine the plateau level of $^{13}$C-glucose in blood while expired breath samples are used to determine the enrichment of $^{13}$CO$_2$. The bicarbonate pool is primed with NaH$^{13}$CO$_3$.

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**Protocol**

**Best Tracer:** U-($^{13}$C$_6$)-glucose  
**Priming Bolus Dose:** 1.1 µmol/kg U-($^{13}$C$_6$)-glucose  
**Priming Bolus Dose:** 0.6 mmol NaH$^{13}$CO$_3$  
**Infusion Pump Speed:** 0.174 cc/min  
**Infusion Rate:** 2.5 µmol/kg/hr  
**Infusion Time:** 140 min.  
**Sampling Times:** 0, 90, 100, 110, 120, 130, 140 min. (Plasma and Breath)  
**Diet Protocol:** Fasted or Fed  
**References:** Wolfe et al., Metabolism 28, 210-219, 1979.  
Robert et al., Diabetes 31, 203-211, 1982.

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**Glucose Synthesis from Precursors**
The rate of gluconeogenesis can be quantified from gluconeogenic substrates using $^{13}$C stable isotope tracers. For example, to quantify the glucose-alanine relationship, one needs to determine the incorporation of alanine carbon into glucose. In addition, the fraction of lactate produced from alanine can be determined by measuring the enrichment of lactate. These studies require the infusion of [2,3-$^{13}$C$_2$]-alanine and 6,6-D$_2$-glucose as tracers.

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**Protocol**

**Best Tracers:** [2,3-$^{13}$C$_2$]-alanine and 6,6-D$_2$-glucose  
**Priming Bolus Dose:** 14 µmol/kg Each tracer  
**Infusion Pump Speed:** 0.174 cc/min  
**Infusion Rate:** 11.5 µmol/kg/hr Each tracer  
**Infusion Time:** 140 min.  
**Sampling Times:** 0, 90, 100, 110, 120, 130, 140 min. (Plasma and Breath)  
**Diet Protocol:** Fasted or Fed  
**References:** Kalhan et al., Metabolism 37, 152-158, 1988.