Placental tissue and cellular metabolism

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Tissue and cellular metabolism

Placental tissue and cell metabolism are crucial functions for study

- Placental metabolic functions are vital for the growth and development of the placental supply line.
- The placenta is metabolically active, consuming a significant fraction of the metabolic substrates it takes up, thus altering output to the fetus
- The placenta also acts as a metabolic sensor. Under abnormal or stress conditions such as hypoxia, placental metabolism is modified resulting in alterations to the substrate profile presented to the fetus

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Pathophysiologies

Intrauterine growth restriction (IUGR), preeclampsia (PE) and diabetes in pregnancy

Pathophysiologic processes

Those that alter the distribution and utilization of energy-generating substrates, primarily oxygen and glucose

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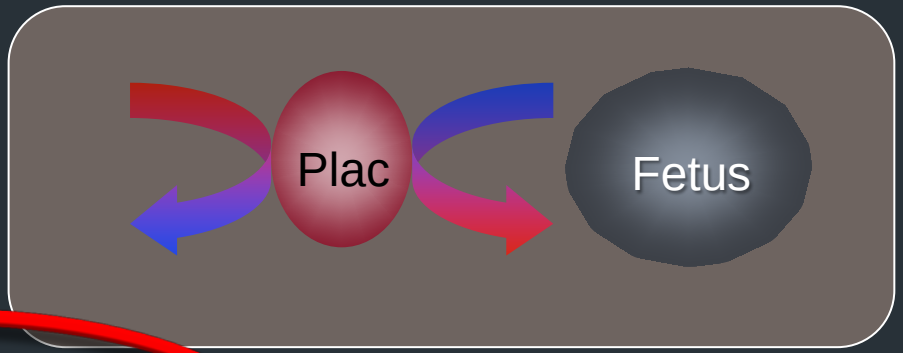
Oxygen:



Reduced uteroplacental blood flow

Hypoxia

Altered placental metabolism

Reactive oxygen species

Oxidatve damage

Intrauterine growth restriction

Preeclampsia

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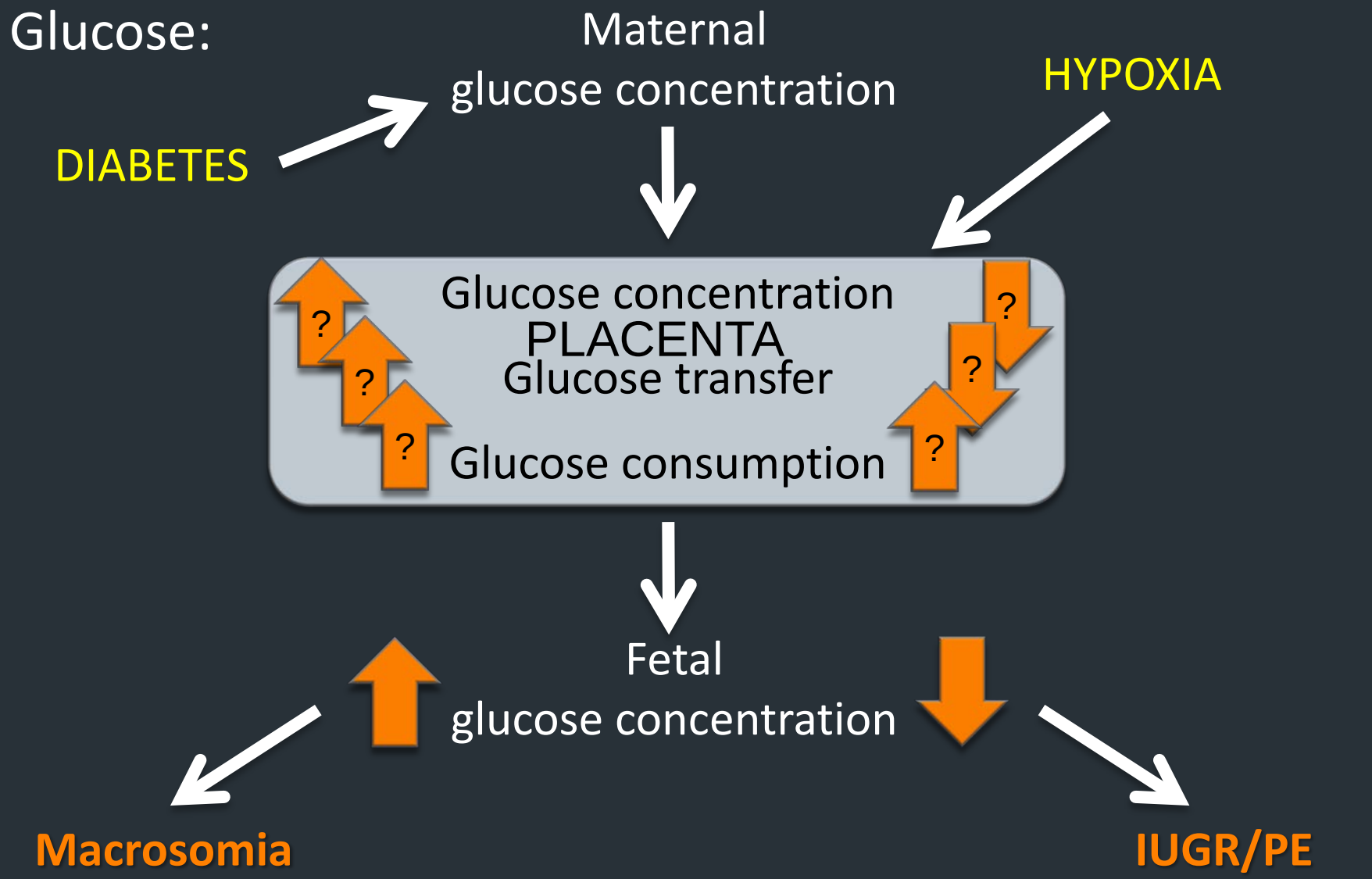

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Pathophysiologic processes

Those that alter the distribution and utilization of energy-generating substrates, primarily oxygen and glucose

What are the sort of questions we need to answer?

- When does placental hypoxia occur? Can we measure intervillous $pO_2$and oxygenation in other placental blood spaces?
- What is placental glycemic status? How can we measure placental glucose transfer and consumption in vivo?
- What is the balance between glycolytic and oxidative energy metabolism in the placenta? Can we measure this in real time?
- When does flow reduction, hypoxia, reperfusion lead to generation of ROS? Can we devise ongoing measures of oxidative stress?

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In what other in vivo conditions is assessment of these pathophysiologic processes important?

- Cardiac conditions such ischemic heart disease
- Cerebral hypoxia/ischemia; hypoxia/reperfusion injury
- Solid tumor development/progression
- Obesity, type 1 and type 2 diabetes mellitus

What methodologies and techniques are used in these conditions?

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Oxygen:

With access to tissue:

Physical: Oximetry, near(mid)-infrared spectroscopy, electrodes, other physical probes

Chemical: 2-nitroimidazoles

With access to blood:

Physical: Electrodes, other physical probes,

Chemical: microRNA, metabolomics

No access:

Physical: MRS/^{1}H-lactate, fMRI/BOLD

Chemical: MRS/^{19}F-fluorocarbons

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Glucose:

With access to tissue:

Physical: Near-infrared spectroscopy, electroenzymatic

Chemical: Phenylboronic acid, Concanavalin-A sensors

With access to blood:

Physical: Electrodes, other physical probes,

Chemical: microRNA, metabolomics, PBA/Con-A sensors

No access:

Physical: MRS/^{1}H-lactate, glucoCEST

Chemical: PET, SPECT

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Conclusions

- It is currently impractical to screen for events which lead to placental metabolic disturbances in the absence of other clues such as prior history
- By the time a pathology such as IUGR is detected clinically, it is probable that significant, irreversible (feto)placental damage has occurred
- It is necessary to devise new methods of in utero assessment which will enable therapeutic intervention prior to the establishment of disease