



# Quiz 30, Glucose and the Brain

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**ZINC**

**Atomic #30**

**Density:**

**7.134gm/cm<sup>3</sup>**

To Q 1



# 1. ALL ARE TRUE REGARDING BRAIN METABOLISM EXCEPT

- a. Energy formation for the brain is derived from a catabolic process which leads to the formation of ATP
- b. Most of the Transport of glucose into the brain requires energy
- c. Ionic homeostasis in the brain required for cellular function requires energy
- d. In the absence of oxygen, anaerobic glycolysis produces 2 molecules of ATP per glucose which is inadequate to meet the brain's energy needs

To Q2



# A. ENERGY PRODUCTION FOR THE BRAIN IS DERIVED FROM A CATABOLIC PROCESS WHICH LEADS TO THE FORMATION OF ATP

This statement is true. The breakdown of glucose in the brain through glycolysis produces pyruvate used in the citric acid cycle to generate NADH. Energy from the transfer of electrons from NADH to  $O_2$  in the mitochondria is used to generate ATP through the process of oxidative phosphorylation. ATP is necessary for cellular function. Unconsciousness may occur if blood glucose levels fall leading to movement of glucose out of the brain.

*Kass, Cotrell Brain metabolism, the pathophysiology of brain injury, and potential beneficial agents and techniques in Cotrell and Young's Neuroanesthesia, 5<sup>th</sup> ed. 2010; Mosby Elsevier, PA*

**Incorrect  
Answer**

[Try  
Again](#)

## B. MOST OF THE TRANSPORT OF GLUCOSE INTO THE BRAIN REQUIRES ENERGY

**Correct!**



This statement is false. GLUT1 receptors expressed in endothelial cells which are part of the blood brain barrier and GLUT3 in neurons are responsible for transporting glucose into the brain through the process of facilitated diffusion. These transporters move glucose down its concentration gradient (from higher to lower concentration), a process which does not require energy.

*Benarroch E, Brain glucose transporters: implications of neurologic disease. Neurology,2014;82:1374-79*

*Kass, Cotrell, Brain metabolism, the pathophysiology of brain injury, and potential beneficial agents and techniques in Cotrell and Young's Neuroanesthesia, 5<sup>th</sup> ed. 2010;Mosby Elsevier, PA*

[Back to Q1](#)

[To Q2](#)

## C. IONIC HOMEOSTASIS IN THE BRAIN REQUIRED FOR CELLULAR FUNCTION REQUIRES ENERGY

This is a true statement. Ionic homeostasis which requires energy in the form of ATP is mandatory for excitatory synaptic transmission in the brain. Mitochondrial derived Na/K ATPase is necessary to pump  $K^+$  ions inside the cells and Na out of cells, thereby preserving the ionic gradient across cells. Changes from the resting membrane potential achieved in large part by Potassium's movement along its concentration gradient (negative resting membrane potential of about 90mV) is necessary for generation of action potentials necessary for normal nerve cell function.

*Kass, Cotrell Brain metabolism, the pathophysiology of brain injury, and potential beneficial agents and techniques in Cotrell and Young's Neuroanesthesia, 5<sup>th</sup> ed. 2010; Mosby Elsevier, PA*

[Try  
Again](#)

**Incorrect  
Answer**

## D. IN THE ABSENCE OF OXYGEN, ANAEROBIC GLYCOLYSIS PRODUCES 2 MOLECULES OF ATP PER GLUCOSE WHICH IS INADEQUATE TO MEET THE BRAIN'S ENERGY NEEDS

This statement is true. Under normal aerobic conditions, glycolysis, the citric acid cycle and finally oxidative phosphorylation will produce 38 ATP per glucose molecule. In the absence of oxygen, anaerobic glycolysis converts pyruvate to lactate regenerating NAD producing only two ATP molecules . ATP is necessary to pump  $K^+$  ions inside the cells and Na out of cells, thereby preserving the ionic gradient across cells. Without these energy dependent pumps, ions would continue to leak down their electrochemical gradients reducing the membrane potential to 0, causing cells to depolarize and die.

*Kass, Cotrell Brain metabolism, the pathophysiology of brain injury, and potential beneficial agents and techniques in Cotrell and Young's Neuroanesthesia, 5<sup>th</sup> ed. 2010; Mosby Elsevier, PA*

[Try Again](#)

**Incorrect  
Answer**

## 2. HYPERGLYCEMIA IN TRAUMATIC BRAIN INJURED (TBI) PATIENTS IS DUE TO ALL OF THE FOLLOWING EXCEPT

- a. Cortisol
- b. Gluconeogenesis
- c. Opioids
- d. Corticotrophin

To Q3



# A. CORTISOL

Intraoperative hyperglycemia common in adults undergoing craniotomy for TBI contributes to secondary brain injury. Hormones like cortisol produced in response to stress contribute to hyperglycemia in these patients. In response to trauma/surgical stress the hypothalamus releases corticotrophin releasing hormone which stimulates the anterior pituitary to release corticotrophin (ACTH) which stimulates the adrenal cortex to release cortisol stimulating gluconeogenesis. Baseline cortisol levels of 400mmol/L may reach maximum levels of 1500 mmol/L.

*Sharma D, Perioperative management of adult traumatic brain injury, Anesthesiology clinics, 2012;30:333-346*

*Desborough JP, The Stress response to trauma and surgery, Br J A, 2000;85(1):109-17*

[Try  
Again](#)

**Incorrect Answer**

## B. GLUCONEOGENESIS

With feedback inhibition of corticotrophin by cortisol suppressed with surgery, cortisol levels are unchecked and this hormone is able to continue promoting gluconeogenesis in the liver exacerbating hyperglycemia

*Desborough JP, The Stress response to trauma and surgery, Br J A, 2000;85(1):109-17*

**Incorrect Answer**

[Try  
Again](#)

## C. OPIOIDS

**Correct!**



Opioids are commonly used in anesthesia in part to suppress hypothalamic and pituitary hormone secretion. Morphine suppresses the release of corticotrophin from the hypothalamus and has also been found to inhibit cortisol release. In cardiac surgery Fentanyl, Sufentanil, and Alfentanil suppress pituitary hormone secretion ultimately limiting glucose production.

*Desborough JP, The Stress response to trauma and surgery, Br J A, 2000;85(1):109-17*

[Back to Q2](#)

[To Q3](#)

## D. CORTICOTROPHIN

In response to trauma/surgical stress, the hypothalamus releases corticotrophin releasing hormone which stimulates the anterior pituitary to release corticotrophin (ACTH) which stimulates the adrenal cortex to release cortisol stimulating gluconeogenesis.

*Desborough JP, The Stress response to trauma and surgery, Br J A  
2000;85(1):109-17*

**Incorrect Answer**

[Try  
Again](#)

### 3. WHICH OF THE FOLLOWING IS **TRUE** REGARDING SERUM GLUCOSE IN PATIENTS WITH INJURED BRAIN

- a. Hypoglycemia has little impact on injured brain
- b. Hyperglycemia is not a problem in patients with cerebral ischemia.
- c. Perioperative hyperglycemia is common in adults but not children undergoing craniotomy for traumatic brain injury.
- d. Patients with intraoperative hyperglycemia during neurosurgical procedures are more likely to develop postoperative neurologic dysfunction.

To Q 4



## A. HYPOGLYCEMIA HAS LITTLE IMPACT ON INJURED BRAIN

In the setting of subarachnoid hemorrhage, traumatic brain injury, and ischemic stroke, hypoglycemia is associated with a worse outcome.

*Kass, Cotrell Brain metabolism, the pathophysiology of brain injury, and potential beneficial agents and techniques in Cotrell and Young's Neuroanesthesia, 5<sup>th</sup> ed. 2010; Mosby Elsevier, PA*

*Stutz, Charchafli, Postoperative intensive care including head injury and multisystem sequelae, in Cotrell and Young's Neuroanesthesia, 5<sup>th</sup> ed. 2010; Mosby Elsevier, PA*

[Try  
Again](#)

**Incorrect Answer**

## B. HYPERGLYCEMIA IS NOT A PROBLEM IN PATIENTS WITH CEREBRAL ISCHEMIA.

In patients with cerebral ischemia, hyperglycemia will exacerbate tissue acidosis and lactate generation exacerbating secondary neuronal injury. This is in part due to conversion of pyruvate to lactate. Hydrogen ions produced in anaerobic glycolysis may also worsen neuronal damage as intracellular pH decreases.

*Kass, Cotrell Brain metabolism, the pathophysiology of brain injury, and potential beneficial agents and techniques in Cotrell and Young's Neuroanesthesia, 5<sup>th</sup> ed. 2010; Mosby Elsevier, PA*

*Stutz, Charchafli, Postoperative intensive care including head injury and multisystem sequelae, in Cotrell and Young's Neuroanesthesia, 5<sup>th</sup> ed. 2010; Mosby Elsevier, PA*

**Incorrect Answer**

[Try Again](#)

## C. PERIOPERATIVE HYPERGLYCEMIA IS COMMON IN ADULTS BUT NOT IN CHILDREN UNDERGOING CRANIOTOMY FOR TRAUMATIC BRAIN INJURY.

Intraoperative hyperglycemia is common in adults undergoing urgent/emergent craniotomy for TBI, with up to 15% of patients experiencing new onset hyperglycemia. Similarly, in a retrospective cohort study evaluating 105 children  $\leq 13$  years for emergency craniotomy for TBI, 17% had persistent hyperglycemia.

*Sharma D, Perioperative management of adult traumatic brain injury, Anesthesiology clinics, 2012;30:333-346*

*Sharma D, et al, Incidence and risk factors for perioperative hyperglycemia in children with traumatic brain injury, Anesth Analg. 2009;108:81-9*

**Incorrect Answer**

[Try Again](#)

D. PATIENTS WITH INTRAOPERATIVE HYPERGLYCEMIA DURING NEUROSURGICAL PROCEDURES ARE MORE LIKELY TO DEVELOP POSTOPERATIVE NEUROLOGIC DYSFUNCTION.

Correct!



In a retrospective examination of 1000 patients from the Intraoperative Hypothermia for Aneurysm Surgery trial database (IHAST) who underwent aneurysm clipping within 14 days of subarachnoid hemorrhage (SAH), Pasternak et al noted that at 3 months after surgery, those with glucose  $>129$ mg/dL were more likely to have impaired cognition and those with glucose  $> 152$  mg/dL were more likely to experience gross neurologic dysfunction as assessed by the national institute of health stroke scale.

*Pasternak J, Hyperglycemia in patients undergoing cerebral aneurysm surgery: its association with long-term gross neurologic and neuropsychological function. Mayo Clin Proc. 2008;83(4):406-17*

Back to Q3

To Q4

4. GLUCOSE CONTROL IS IMPORTANT IN ORDER TO LIMIT SECONDARY BRAIN INJURY. ALL OF THE FOLLOWING ARE TRUE REGARDING THE MANAGEMENT OF GLUCOSE LEVELS **EXCEPT.**

- a. Maintaining serum glucose  $\leq 180$  mg/dl ( $\leq 10$ mmol/L) is reasonable in order to avoid extremes of glucose in TBI patients.
- b. Intensive insulin therapy carries an increased risk of death
- c. Intensive insulin therapy carries an increased risk of hypoglycemia
- d. Tight glucose control between 80 and 110mg/dl is recommended in critically ill patients

To Q5

## A. MAINTAINING SERUM GLUCOSE $\leq 180$ MG/DL ( $\leq 10$ MMOL/L) IS REASONABLE IN ORDER TO AVOID EXTREMES OF GLUCOSE IN TBI PATIENTS.

This statement is true. In a retrospective cohort study of 170 patients admitted to the ICU with traumatic brain injury (GCS $\leq 8$ ), episodes of hyperglycemia (glucose  $\geq 200$ mg/dl or  $\geq 11.1$ mmol/L) during the first 10 days after injury was associated with a 3.6 fold increased risk of in-hospital mortality. Authors of this study concluded that while more studies are needed to determine the optimal glucose range, they recommend keeping glucose  $\leq 180$  mg/dl ( $\leq 10$ mmol/L) in TBI patients.

*Griesdale DE, Glucose control and mortality in patients with severe traumatic brain injury. Neurocrit Care, 2009;11:311-16*

**Incorrect Answer**

[Try Again](#)

## B. INTENSIVE INSULIN THERAPY CARRIES AN INCREASED RISK OF DEATH

This statement is true. In a prospective trial of ICU patients randomized to intensive glucose control (glucose 80-110 mg/dL) vs conventional blood glucose control (insulin therapy started when glucose >215mg/dL and therapy decreased once glucose <180mg/dL), logistic regression analysis did identify hypoglycemia as an independent risk factor for death compelling consideration of this factor influencing the potential benefit of intensive insulin therapy.

*Van den Berghe G, et al Intensive insulin therapy in the medical ICU, 2006;354(5):449-61*

Incorrect  
Answer

[Try  
Again](#)

## C. INTENSIVE INSULIN THERAPY CARRIES AN INCREASED RISK OF HYPOGLYCEMIA

This statement is true. In a prospective study of 97 patients with severe traumatic brain injury randomized to traditional insulin therapy for glucose levels >220 mg/dl or more intensive therapy with glucose goals of between 80 and 120 mg/dl, Bilotta et al noted that the intensive insulin therapy group had significantly more hypoglycemic episodes. A benefit of intensive insulin therapy included a shorter ICU stay, however both groups had similar mortality and neurologic outcome.

*Bilotta et al, Intensive insulin therapy after severe traumatic brain injury: a randomized clinical trial, Neurocrit Care. 2008;9:159-166*

**Incorrect Answer**

[Try Again](#)

**Correct!**



## D. TIGHT GLUCOSE CONTROL BETWEEN 80 AND 110MG/DL IS RECOMMENDED IN CRITICALLY ILL PATIENTS

In a large, international, randomized trial where 3016 intensive care patients received intensive-control of blood glucose (target of 81-108 mg/dl) vs 3014 patients who received a more conventional glucose management (target < 180 mg/dl), investigators found an increased mortality in the intensive-control group of patients (27.5%) compared to the conventional group (24.9%). Despite the negative consequences of hyperglycemia like metabolic acidosis and neuronal cell death, tight glucose control can be harmful. It is more reasonable to keep glucose between 100-150 mg/dl (5.5-8.25mmol/dl) or 80-180mg/dl during the perioperative period.

*Nice Sugar study investigators, Intensive vs conventional glucose control in critically ill patients, NEJM, 2009;360(13):1283-97*

*Stutz, Charchafli, Postoperative intensive care including head injury and multisystem sequelae, in Cotrell and Young's Neuroanesthesia, 5<sup>th</sup> ed. 2010;Mosby Elsevier, PA*

*Sharma D, Perioperative management of adult traumatic brain injury, Anesthesiology clinics, 2012;30:333-346*

[Back to Q4](#)

[To Q5](#)

## B. HYPERGLYCEMIA IS ASSOCIATED WITH POOR OUTCOME AFTER TBI IN CHILDREN.

In an effort to understand the relationship between hyperglycemia and severe TBI in children, Smith et al prospectively followed serum glucose levels in children with severe TBI (GCS  $\leq 8$ ) with protocol based care which excluded glucose administration for 48 hours after TBI unless serum glucose  $< 70$  mg/dL. At  $> 48$  hours, these authors found an association between increased serum glucose ( $> 133$  mg/dL) and unfavorable outcome, as determined by Glasgow outcome scores at 6 months vs a more favorable outcome in children with glucose  $< 115$  mg/dL.

*Smith RL, Relationship between hyperglycemia and outcome in children with severe traumatic brain injury, Pediatr Crit Care Med. 2012;13:85-91*

**Incorrect Answer**

[Try Again](#)

5. ALL OF THE FOLLOWING STATEMENTS ARE TRUE REGARDING HYPERGLYCEMIA AND TBI IN CHILDREN EXCEPT

- a. Age <4 years and severe TBI are risk factors for perioperative hyperglycemia in children.
- b. Hyperglycemia is associated with poor outcome after TBI in children.
- c. Severe Hyperglycemia in children with traumatic brain injury is associated with increased mortality
- d. Administration of dextrose containing intravenous solutions are routine in pediatric TBI patients

← Back to Q1

## A. AGE <4 YEARS AND SEVERE TBI ARE RISK FACTORS FOR PERIOPERATIVE HYPERGLYCEMIA IN CHILDREN.

Data from a retrospective cohort study of 105 children  $\leq 13$  years who underwent craniotomy for TBI none of whom received perioperative steroids or dextrose in their IV fluids before and during surgery revealed that perioperative hyperglycemia is common. Some risk factors for perioperative hyperglycemia in this group of TBI patients were age <4 years, severe TBI (GCS $\leq 8$ ), isolated subdural hematoma (SDH), and multiple lesions on head CT.

*Sharma D, Incidence and risk factors for perioperative hyperglycemia in children with traumatic brain injury, A and A. 2009;108:81-89*

**Incorrect Answer**

[Try Again](#)

## C. SEVERE HYPERGLYCEMIA IN CHILDREN WITH TRAUMATIC BRAIN INJURY IS ASSOCIATED WITH INCREASED MORTALITY

In a retrospective study of 271 Children admitted to the intensive care with moderate-to severe traumatic brain injury, more children with severe blood glucose elevation ( $>200\text{mg/dL}$  or  $11\text{mmol/L}$ ) died compared to children with lower blood glucose levels ( $<200\text{ mg/dL}$ )

*Elkon B, et al. Hyperglycemia, and independent risk factor for poor outcome in children with traumatic brain injury. Pediatric Crit Care Med 2014;15(7):623-631*

**Incorrect Answer**

[Try Again](#)

## D. ADMINISTRATION OF DEXTROSE CONTAINING INTRAVENOUS SOLUTIONS ARE ROUTINE IN PEDIATRIC TBI PATIENTS

Glucose is not routinely added to maintenance fluids in children with TBI due to the frequency and consequences of stress induced hyperglycemia.

*Agrawal S, Neuroprotective measures in children with traumatic brain injury, World J of Crit Care Med, 2016;5(1):36-46*



**Correct !**

← **Back to Q5**

**End of Set**

**Back To Q 1** →