

## Topic 36: ASSIMILATION AND FASTING

### I Assimilation

A Definition: Incorporation of nutrients into body

B Purpose

C Control systems

1 Insulin

a made in beta cells of pancreatic islets

b promotes glucose utilization by cells during times of high glucose availability

2 Glucagon

a made in alpha cells of pancreatic islets

b promotes return of glucose to blood

3 Why needed

a prevent hypoglycemia during fasting – brain especially needs glucose

b promote efficient utilization of glucose when it is absorbed

c maintain adequate levels of circulating glucose, fats, and amino acids

### II The Fed State

A Increase in blood glucose levels stimulates release of insulin

B Effects of insulin

1 Liver: promotes uptake of glucose and amino acids

a glucose → glycogen

b amino acids → protein

c excess glucose → fatty acids

d excess amino acids → fatty acids

2 Muscle: promotes uptake of glucose and amino acids

a glucose → glycogen

b amino acids → protein

3 Adipose tissue: inhibits fat breakdown and promotes fat uptake

a fatty acids (from diet and from metabolic conversion in liver) → triglycerides

4 All other tissues: promotes uptake of glucose

### III The Fasting State

- A Decrease in blood glucose levels stimulates release of glucagon, inhibits release of insulin
- B Effects of glucagon/low insulin
  - 1 Liver: promotes release of glucose by:
    - a glycogen → glucose
    - b protein → amino acids → glucose (gluconeogenesis)
  - 2 Adipose tissue: promotes release of free fatty acids
    - a triglycerides → fatty acids

### IV Special Case: a very high protein meal

- A Increase in blood amino acids stimulates release of glucagon and insulin
- B Insulin promotes uptake of amino acids by tissues
- C Glucagon counteracts insulin's effects on blood glucose to prevent hypoglycemia

### V Special Case: starvation

- A Liver glycogen stores are depleted in about 15 hours of not eating
- B Prolonged low blood glucose stimulates release of glucagon AND cortisol
- C In the first few days, proteins in muscles broken down into amino acids for gluconeogenesis
- D Fat in adipose broken down into free fatty acids for all tissues but brain – body weight diminishes rapidly
- E FFAs converted into ketones (keto-acids) in liver – brain can use these in emergencies to spare valuable protein from conversion into glucose
- F Beyond a few days, thyroid hormone (T3) decreases, BMR slows so that body weight diminishes by very little per day

VI Special Case: prolonged exercise

- A Brief exercise uses immediate sources of glucose (ATP and creatine phosphate)
- B Low blood glucose and sympathetic activity stimulate release of glucagon
- C Long-term exercise (5 min - 1 hour) uses circulating glucose liberated from muscle and liver glycogen stores (promoted by glucagon)
- D Really long-term exercise (1 - 4 hours) still uses circulating glucose but muscles begin to rely on free fatty acids
- E At 4 hours or so, muscles use  $\frac{2}{3}$  FFAs and  $\frac{1}{3}$  glucose; much of glucose reserved for the brain

## Topic 37: ENERGY BALANCE AND THERMOREGULATION

### I Energy Balance

A Input = Output

B Animal energy equation:

1 Output = Self maintenance + Feeding + Activity + Production + Heat

a Self maintenance = BMR

b Feeding = energy needed to obtain/consume/digest food

c Activity = exercise

d Production = growth (including fat storage), reproduction

e Heat = "waste heat" (can be >50% of output)

2 Input = Food

C On the molecular level:

1 output = catabolism + work

2 work = anabolic work + transport work + mechanical work

3 anything that requires ATP or similar molecule as an energy source = output

### II Control of Input

A Hypothalamus contains "feeding centers" and "satiety centers"

1 Lipostatic theory

a Fat storage signals satiety

b Adipose tissue releases leptin (a peptide hormone)

c cells in hypothalamus have leptin receptors

2 Glucostatic theory

a insulin released from pancreas in response to increase in blood glucose

b increased level of insulin in blood signals satiety to hypothalamus

3 Other possibilities

a Ratio of ATP/ADP

b CCK may signal satiety

c Neurotransmitters: serotonin

C When input is poorly controlled: obesity

1 Obesity = 22% in U.S. are obese compared to "normal standards"

2 Input > Output, remainder stored as fat ("production")

3 Possible causes:

a Hypothalamic control abnormal

i Cells less sensitive to leptin because of different leptin receptors

ii Leptin hormone is different or absent ?

- b other endocrine disorders (hypothyroidism)
- c Input > Output!

### III Control of Output (heat)

- A Heat generated as a result of metabolic processes must be controlled to maintain thermal homeostasis
  - 1 Core temperature maintained at approx. 100 deg. F
  - 2 Temp can vary a bit
    - a time of day: low in morning, high in early evening
    - b time of menstrual cycle: temp higher in second half of cycle
    - c exercise: can be as high as 104 deg. F
    - d fever: to make internal environment incompatible with pathogen
  
- B Heat gain (metabolism and environment) must balance heat loss (to environment)
  - 1 Heat transfer mechanisms
    - a radiation: transfer of heat from warm objects (or air) to cooler ones
    - b conduction: transfer of heat between objects that are in direct contact
    - c convection: transfer of heat energy by air or water currents
    - d evaporation: heat is used to transform water from liquid to gas – this heat is absorbed from the body surface
  
  - 2 Heat loss occurs by all 4 mechanisms
    - a radiative and evaporative cooling are regulated by hypothalamus
    - b sympathetic NS activity increases
      - i vasodilation of skin-surface arterioles: flow increases: more radiative cooling
      - ii sweating: will only work if sweat can evaporate; if humidity is high, sweat will not evaporate
  
  - 3 Heat gain can occur by the first 3 mechanisms plus a few others
    - a mechanical thermogenesis
      - i shivering: rhythmic contractions of skeletal muscles
      - ii reflex activities like foot-stomping and hand-clapping
    - b nonmechanical thermogenesis
      - i brown adipose tissue (BAT) – in response to thyroid hormone and/or NE, these cells literally “burn” fat
      - ii mitochondria in BAT are uncoupled: H<sup>+</sup> leak back through inner mitochondrial membrane without generating ATP

- iii most important in newborns
- iv present in adults?
- c nonexercise activity thermogenesis (NEAT)
  - i probably not for regulating body temp but for regulating energy balance
  - ii “fidgeting”
  - iii people who don’t gain weight even when overfed tend to fidget more!

## IV Thyroid Gland

- A Review structure
  - 1 Two lobes of endocrine tissue joined by isthmus; looks like bowtie
  - 2 Located over the trachea below the larynx
  - 3 Secretory cells, also called follicular cells, are arranged into hollow spheres called follicles
  - 4 Inside of follicles filled with colloid, which is the thyroid hormone synthesis and storage site.
  
- B Synthesis of T3 and T4
  - 1 Tyrosine, an amino acid, can be synthesized by body
  - 2 Iodine must be ingested
    - a actively transported against steep concentration gradient into thyroid gland.
  - 3 Two thyroid hormones synthesized within the colloid
    - a T3: triiodothyronine (triiodo means 3 iodines)
    - b T4: tetraiodothyronine (tetraiodo means 4 iodines)
  
- C T3 and T4 in the Blood
  - 1 90% of thyroid hormone released is T4, BUT
  - 2 T3 is far more functionally potent
  - 3 Most of secreted T4 is converted to T3 by cells at the site of its activity
  - 4 T3 and T4 in blood are bound to plasma proteins
  
- D Regulation of Thyroid function
  - 1 Hypothalamus secretes Thyrotropin releasing hormone (TRH)
  - 2 TRH stimulates anterior pituitary to produce Thyroid stimulating hormone (TSH) – this is the tropic hormone
  - 3 TSH stimulates thyroid to produce T3 and T4 (which are non-tropic hormones)
  - 4 Increased T3 and T4 reduce production of TSH (negative feedback loop)
  
- E Effects of T3 and T4
  - 1 Tends to be slow acting; takes hours or days to see effects of increased levels
  - 2 Metabolic Rate: Increases
  - 3 Heat Production: Increases
  - 4 In general, very high levels of T3/T4 tend to favor consumption, rather than storage, of fuel
  - 5 Sympathetic nervous system: E and NE are more effective when T3 is around

6 Required for CNS development, and CNS function in adults

- F Abnormalities of thyroid function
  - 1 Hypothyroidism from birth
  - 2 Hypothyroidism in adult
    - a Causes
    - b Symptoms
    - c Treatment
  - 3 Hyperthyroidism
    - a Causes
    - b Symptoms
    - c Treatment

## Topic 38: DIABETES/HELP SESSION FOR EXAM IV

### I Diabetes mellitus

A symptoms due to inadequate insulin action = “exaggerated fasting state”

- 1 type I diabetes = lack of insulin secretion
  - a onset in childhood
  - b 10-20% of all diabetics are type I
  - c results from autoimmune destruction of pancreatic beta cells?
  - d not associated with obesity
  
- 2 type II diabetes = reduced sensitivity to insulin in target cells
  - a onset in adulthood
  - b 80-90% of all diabetics are type II
  - c results from down-regulation of insulin receptors in association with chronic overeating?
    - i overeating results in secretion of increased amounts of insulin to facilitate storage of excess nutrients
    - ii high level of insulin results in decrease in number of insulin receptors
  - d additional “popular” theory: a diet high in refined sugar especially taxes endocrine system
  
- 3 gestational diabetes
  - a may occur in the last 3 months of pregnancy (5% of all pregnancies!)
  - b hCS has a "blocking effect" of insulin on their target cells
  - c in genetically predisposed individuals, pancreatic beta cells can't make enough insulin to make up the difference

B Acute effects of insulin deficiency

- 1 Effects on carbohydrate metabolism
  - a low glucose uptake and increased glucose output from liver result in hyperglycemia
  - b glucose filtered through glomerulus exceeds the capacity of kidney tubules to reabsorb; result is glucose in the urine -- increased osmolarity of urine leads to osmotic diuresis (frequent urination)
  - c loss of fluid causes increase in ECF osmolarity and

- decrease in blood volume
- d can cause cell shrinkage and nervous system malfunction resulting in coma; death
- e reduction in blood volume can cause low cerebral blood flow and/or renal failure due to inadequate filtration pressure; both of these can cause death

- source
- 2 Effects on fat metabolism
    - a triglyceride synthesis is inhibited and fatty acid mobilization is stimulated, resulting in high levels of circulating fatty acids
    - b fatty acids are used by tissues as an alternative energy
    - c liver converts fatty acids to ketones (ketosis) -- breath smells "fruity"
    - d ketones are acidic, ketosis results in metabolic acidosis
    - e compensated by chemical buffers, increased respiratory activity, and by secretion of H<sup>+</sup> and reabsorption of HCO<sub>3</sub><sup>-</sup> by kidney
    - f but if filtration rate is low (see above), kidneys can't keep up; acidosis leads to coma and death

- weight
- 3 Effects on protein metabolism
    - a protein degradation is stimulated and amino acid uptake is inhibited, resulting in high levels of circulating amino acids
    - b muscles waste away -- children don't grow, and adults lose
    - c increased circulated amino acids used by liver for gluconeogenesis; contributes to hyperglycemia

- C Chronic effects of insulin deficiency
- 1 Cardiovascular
    - a some blood vessels walls thicken
    - b heart disease and stroke
    - c vascular lesions form in kidneys and retina
      - i kidney failure
      - ii diabetic retinopathy; blindness
    - d impaired delivery of blood to extremities

- i infected tissues become gangrenous
    - ii amputation necessary
  - 2 Nervous system -- dysfunction of brain, spinal cord, and peripheral nerves

## II Management of diabetes

- A Type I
  - 1 Insulin injections
  - 2 Dietary: management of carbohydrate intake, complex vs. simple carbs
  - 3 Exercise
- B Type II
  - 1 Dietary control
  - 2 Exercise and weight reduction
- C Gestational
  - 1 Dietary management and exercise are usually sufficient
  - 2 Birth -- no more placental hormones!