AA 1

Thursday, October 23, 2014
9:53 AM

Learning Objectives:
- role of AAs in metabolism
- sources of AAs
- nitrogen metabolism
- final steps in AA degradation (fate of C skeleton)
- how/why proteins are degraded

Nitrogen Cycle
- N_2 fixation (N_2-->NH_3)
  - only carried out by few microorganisms/plants
  - lightning discharges = 10%
- (NH_3-->N_2) & entry into food chain

(GD) (GS)
aKG <----------> Glu ========== Glutamine
NH_4^+ NH_4^+ (G)

**GLUTAMINE = main NH_4^+ carrier*

Role of AAs in Metabolism
- protein synth (400g/day)
- fuel source (20% energy from protein)
- precursors (neurotransmitters, porphyrins, nucleotides)

AA Sources
- protein degradation/turnover (75% recycled)
- diet (supply of N & precursors)
- synthesis (makes diet less important)

AA Degradation (C Backbone Fate)

Classification	Involved in...	Intermediates	AAs
GLUCOGENIC	Gluconeogenesis	- Pyruvate - Oxaloacetate - aKG - Succinyl CoA - Fumarate	many (+ "both")
KETOGENIC	CAC	- Acetyl-CoA/Acetoacetyl-CoA	Leu, Lys (+ "both")
Both			Ile, Phe, Trp, Tyr

Carbon Backbone Sources:

(AT)
Alanine + aKG <------> Pyruvate + Glu

(SD)
Serine ----------> Pyruvate

Dietary Requirements
*AA in = AA out // N in = N out
- 9 ESSENTIAL AAs - C skeletons cannot be synthesized by body & must be replaced via diet

Any	Arg	(Urea Cycle), children
Help	His	
In	Ile	
Learning	Leu	
These	Thr	
Little	Lys	
Molecules	Met	need lots to make Cys
Proves	Phe	needs lots to make Tyr
Truly	Trp	
Valuable	Val	

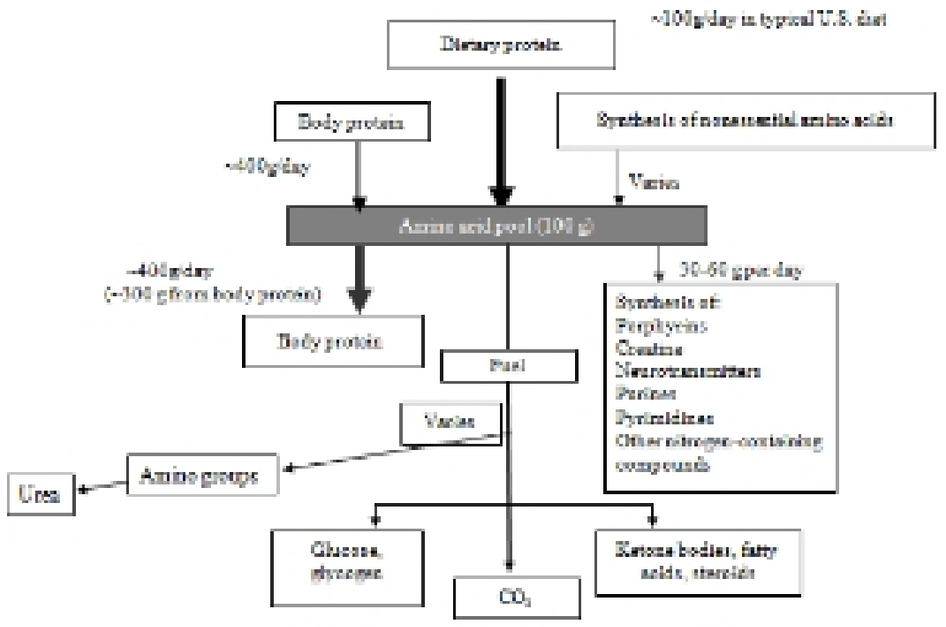
- NON-ESSENTIAL AAs - made from intermediates of Glycolysis, CAC, PPP
- **Adult Protein Requirements:**
  - calculated from TOTAL EXCRETED NITROGEN/24hrs = Urea + NH_3 + Cr + Urate
  - $\frac{(10\ \text{mmoles } N_2)}{\text{kg}} = \frac{(140\ \text{mg } N_2)}{\text{kg}} = \frac{(1\ \text{g protein})}{\text{kg}}$

**Upper Limit: set by capacity of liver to convert to urea*
**US: typically consumes more than daily requirement*

Nitrogen Balance

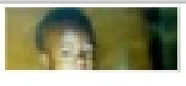
Positive	In > Out	- children - pregnancy - tissue injury repair - Newborn: requires 5x more than adults
Negative	Out > In	**catabolic response of breakdown of proteins to use C skeleton for energy* - infection/sx/trauma/stress - malnutrition (Marasmus/Kwashiorkor) - seen in hospitals - ↓ AA intake, due to Urea Formation Defects (genetic, Liver, Kidney diseases)

AA Intake & Degradation



****determines NITROGEN BALANCE**

Malnutrition:

MARASMUS	KWASHIORKOR (developing countries)
	

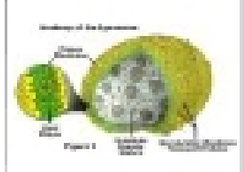
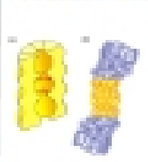
High-Quality Proteins (based on Essential AAs)	Low-Quality Proteins
- breastmilk - meat - fish - yogurt - beans (soy beans)	- jello - maize

Protein Degradation

- continuous	**necessary to eliminate damaged proteins (all-inclusive, not specific for damaged ones)*
- regulated	**via rate-limiting enzymes*
- removal of excess proteins	
- goal-directed	**for energy* **can be cytokine-induced in immune response (NEGATIVE)*

Protein + Calories	Protein
- stunted growth - ↓adipose - ↓protein mass	- stunted growth - fatty liver - ↓albumin - edema
- lethargy - severe wasting - death	- lethargy

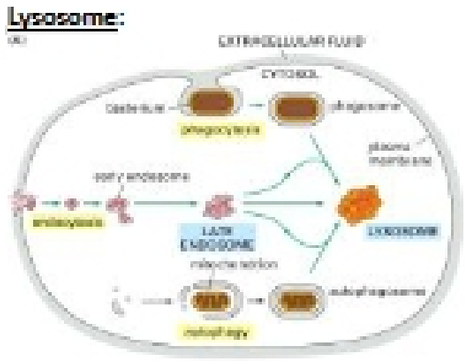
Cell Components for Protein Degradation

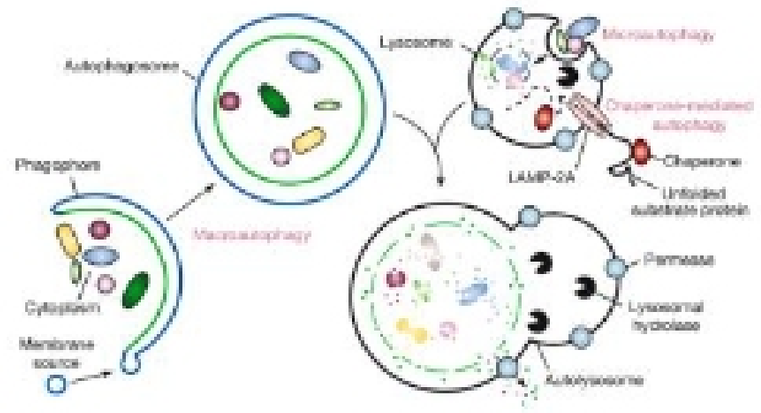
Lysosomes 	cytoplasm	- endocytosis & autophagy of membrane-bound proteins with long half-lives - contain 50 hydrolytic enzymes - acidic environment - AAs released into cytoplasm - NOT highly regulated
Proteasomes 	cytoplasm & nucleus	- huge protein complex that degrades proteins marked by poly-ubiquitin tag 1) 19S - denaturation of tagged proteins (ATP-dependent) 2) Trypsin-like, Chymotrypsin-like, Caspase-like - feed proteins into core 3) small peptides (8-14) - released to be digested by proteases - highly regulated - determined by phosphorylation & AA sequences

AUTOPHAGY - delivery from cytoplasm to lysosome for degradation
- CHAPERONE-MEDIATED - chaperone binds to protein & helps it enter
- MICRO - direct engulfment
- MACRO - double-membrane wraps around protein; basal; in response to environmental signals (malnutrition, hormones, pathogens)

UBIQUITIN - E1, E2[x], E3[x]
**many forms of E2 & E3 for specificity*
**sequences control rate of protein degradation*

Lysosome:





Protease: