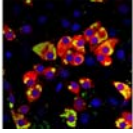


Understanding metabolism in severe malnutrition: from cellular mechanisms to improved child survival



Robert Bandsma
NASPGHAN Annual Meeting
Nestle Nutrition Grant
October 9, 2015



Disclosure slide

In the past 12 months, I have had no relevant financial relationships with the manufacturer(s) of any commercial product(s) and/or provider(s) of commercial services discussed in this CMEactivity.

The role of malnutrition in childhood mortality

- About 45% of all child deaths are linked to malnutrition.
- Severe malnutrition contributes to 516 000 child deaths annually.
- Profound diarrhea or hypoglycemia common direct causes of death in SAM.

Black et al, Lancet 2013
Heikens et al, Lancet 2008

The two forms of severe malnutrition



Marasmus



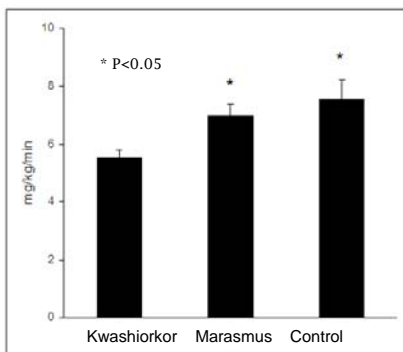
Kwashiorkor

Metabolic dysadaptation in severe malnutrition

- Electrolyte disturbances
- Hypoalbuminemia especially in kwashiorkor
- Abnormal glucose concentrations common:
 - Glucose absorption impaired *
 - Glucose clearance affected #
 - Impaired glucose production
- Fatty liver in kwashiorkor

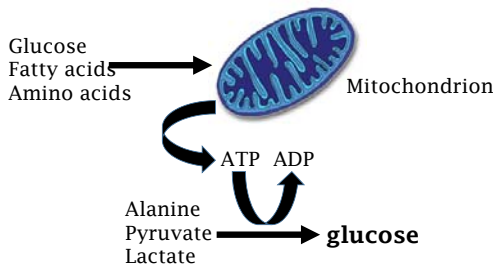
*J Ped 2010
Metabolism 2012*

Glucose production is reduced in children with severe acute malnutrition



Ped Res 2011

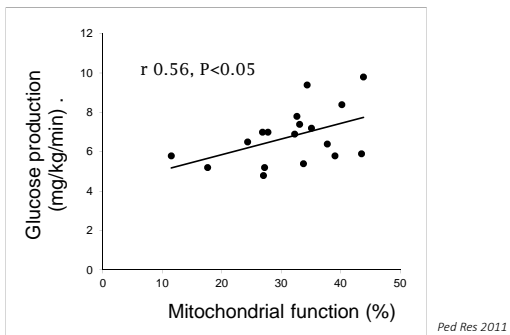
The regulation of hepatic glucose production



Assessing mitochondrial function using isotope breath testing

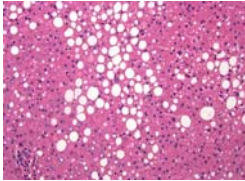


Liver glucose production is correlated with hepatic mitochondrial function

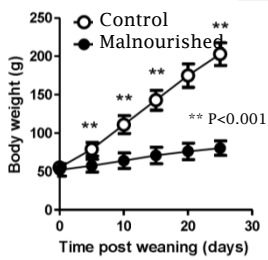


Aim

- To understand the hepatic metabolic dysfunction in severe malnutrition.



Development of an animal model of severe malnutrition



Severe fatty liver in an animal model of malnutrition

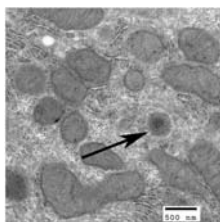


Control

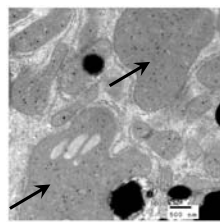


Malnourished

Malnutrition is associated with proliferation of abnormal hepatic mitochondria

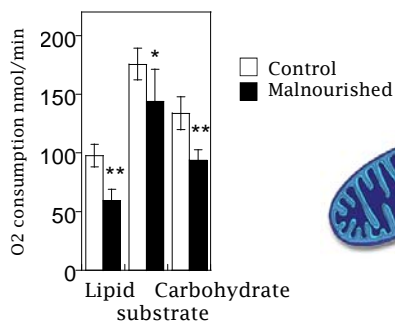


Control

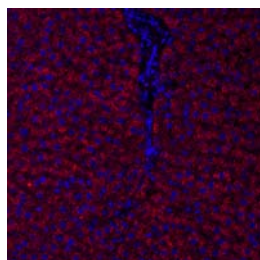


Malnourished

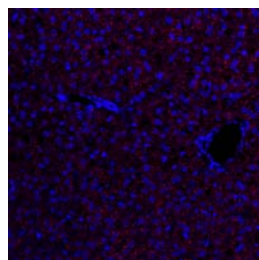
Impaired mitochondrial function in malnutrition



Malnutrition is associated with a loss of hepatic peroxisomes

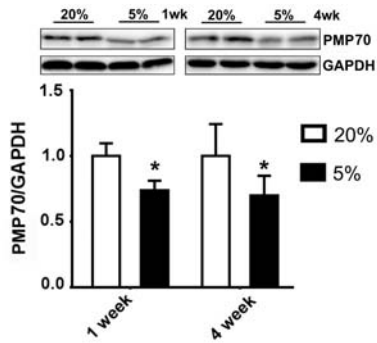


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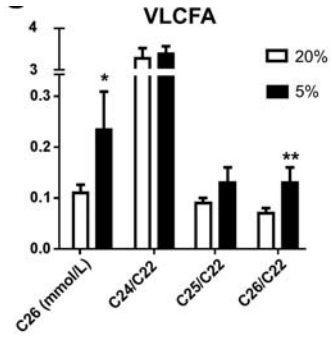


Malnourished

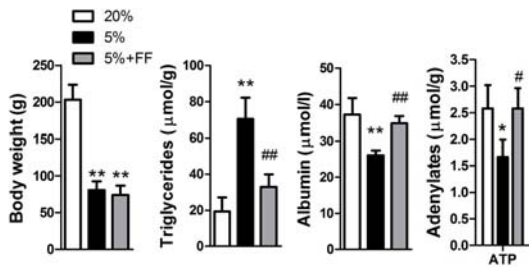
Malnutrition is associated with a loss of hepatic peroxisomes



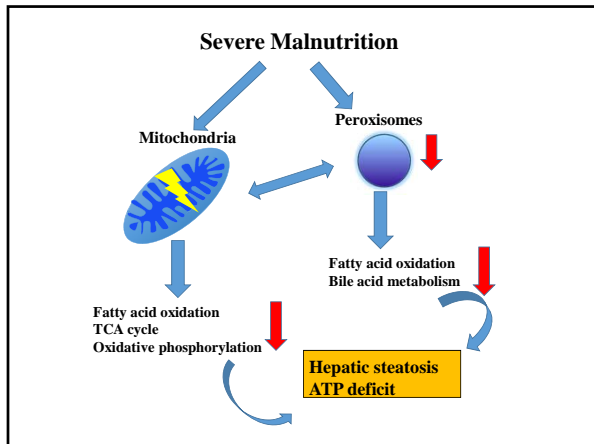
Malnutrition is associated with a loss of hepatic peroxisomal function

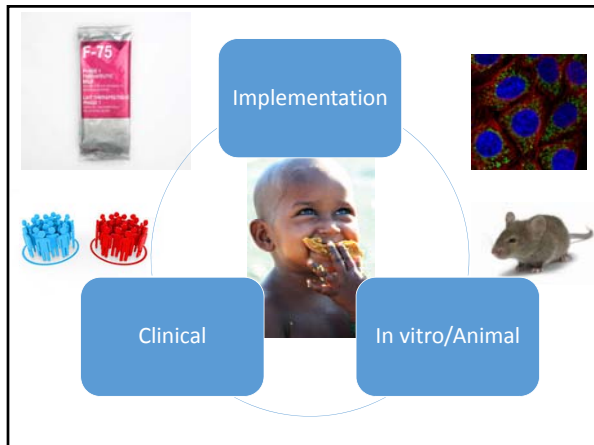


Fibrate treatment improves steatosis and ATP content in malnutrition



Fibrates (FF) are PPAR-alpha agonists, stimulating peroxisome biogenesis and mitochondrial lipid oxidation





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