

Understanding Choline: An Overlooked Nutrient in Pigs and Chickens



Ryan N. Dilger, PhD

University of Illinois at Urbana-Champaign

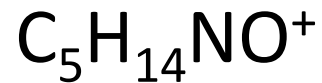
Department of Animal Sciences

Division of Nutritional Sciences

Neuroscience Program

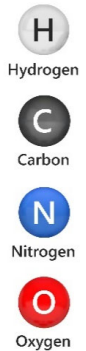
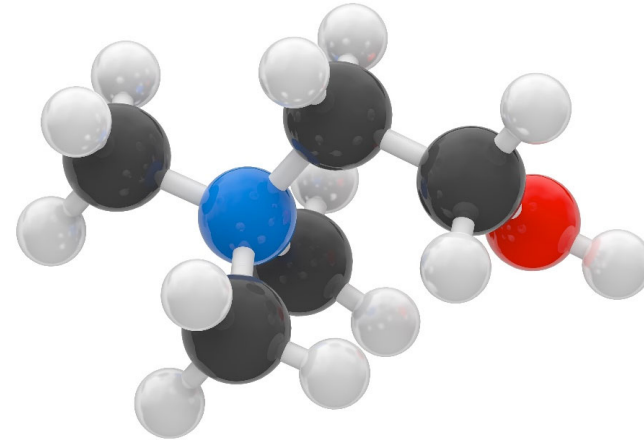
Balchem Real Science Lecture Series, February 23, 2021

Choline



104.1708 g/mol

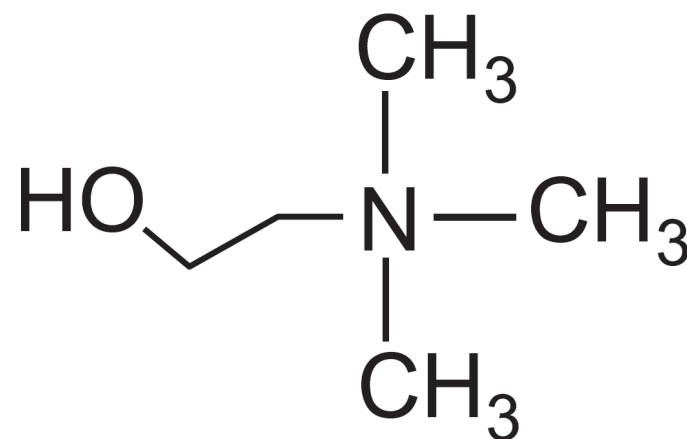
Discovered by Adolph Strecker in 1862 as isolated from pig and ox bile ('chole' in Greek)



Outline

- Choline functions and metabolism
- Clinical signs of deficiency
- Feedstuff concentrations and relative bioavailability
- Pigs vs. chickens: requirements and metabolic idiosyncrasies

- 2-hydroxyethyl-trimethyl-ammonium salt
- Quasi-vitamin (high concentrations, *de novo* synthesis) and conditionally essential nutrient
- Defined as an essential nutrient for humans in 1998 (Institute of Medicine, IOM)
- Choline-containing metabolites and derivatives critical for multiple functions
- Can be synthesized endogenously
- Present in the diet in various forms



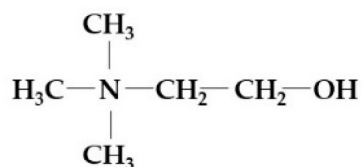
Choline

(*N*-trimethylethanolamine)

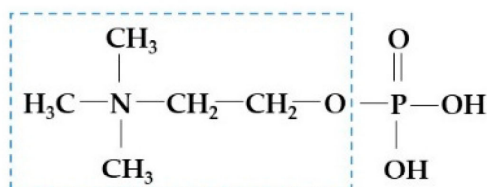
Forms of Choline



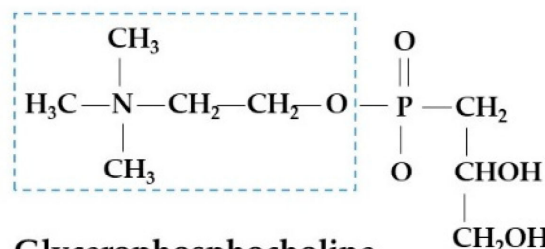
Water-soluble forms



Choline



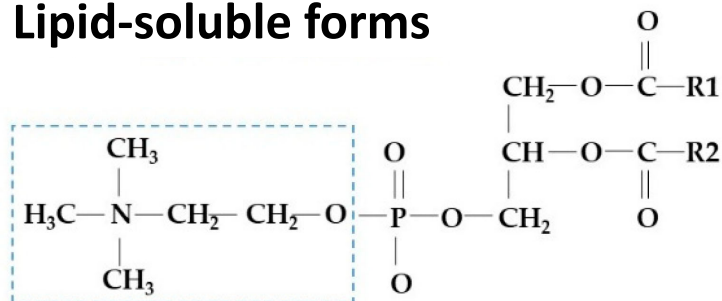
Phosphocholine



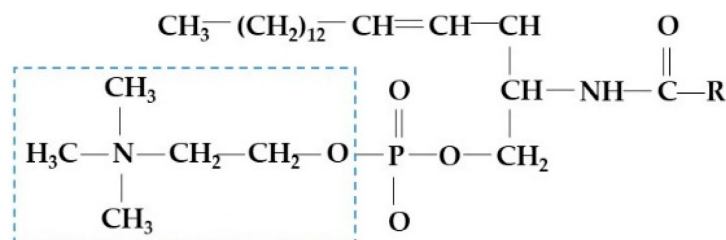
Glycerophosphocholine

- Reach the liver via portal circulation

Lipid-soluble forms



Phosphatidylcholine



Sphingomyelin

- Packaged into chylomicrons and transported via lymphatic system

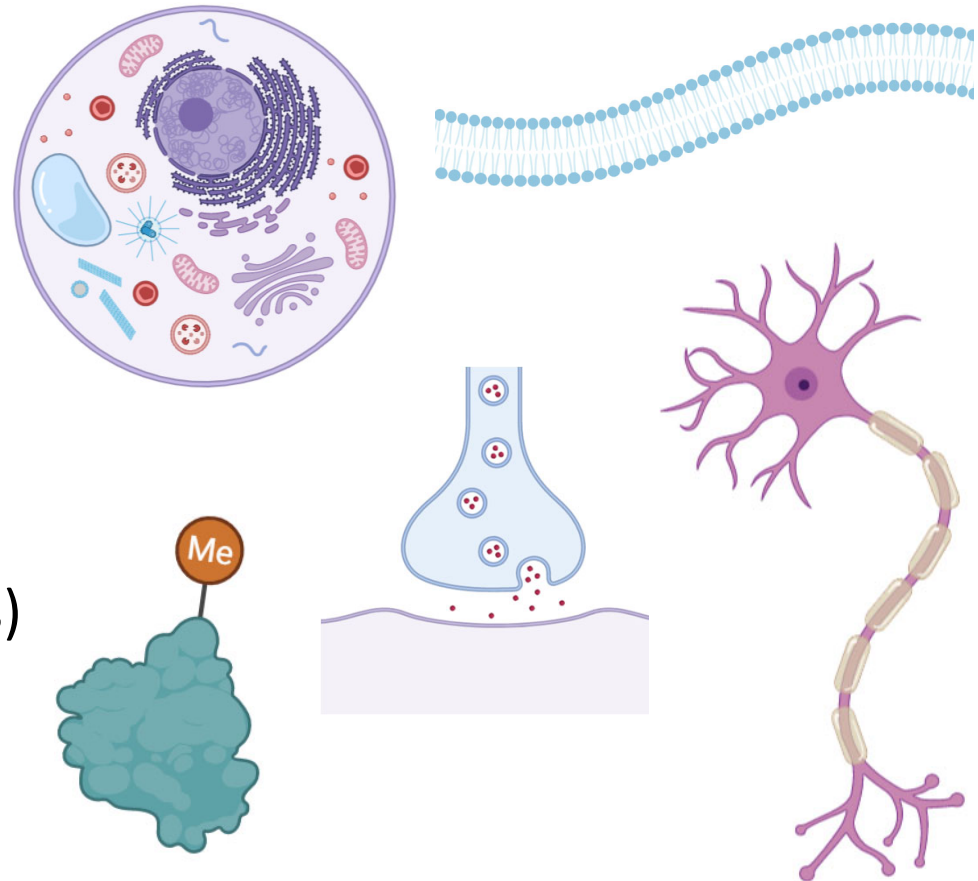
Blue-dotted box denotes choline (per se) as incorporated into other forms

Wiedeman et al., 2018; Nutrients 10, 1513

Choline Functions



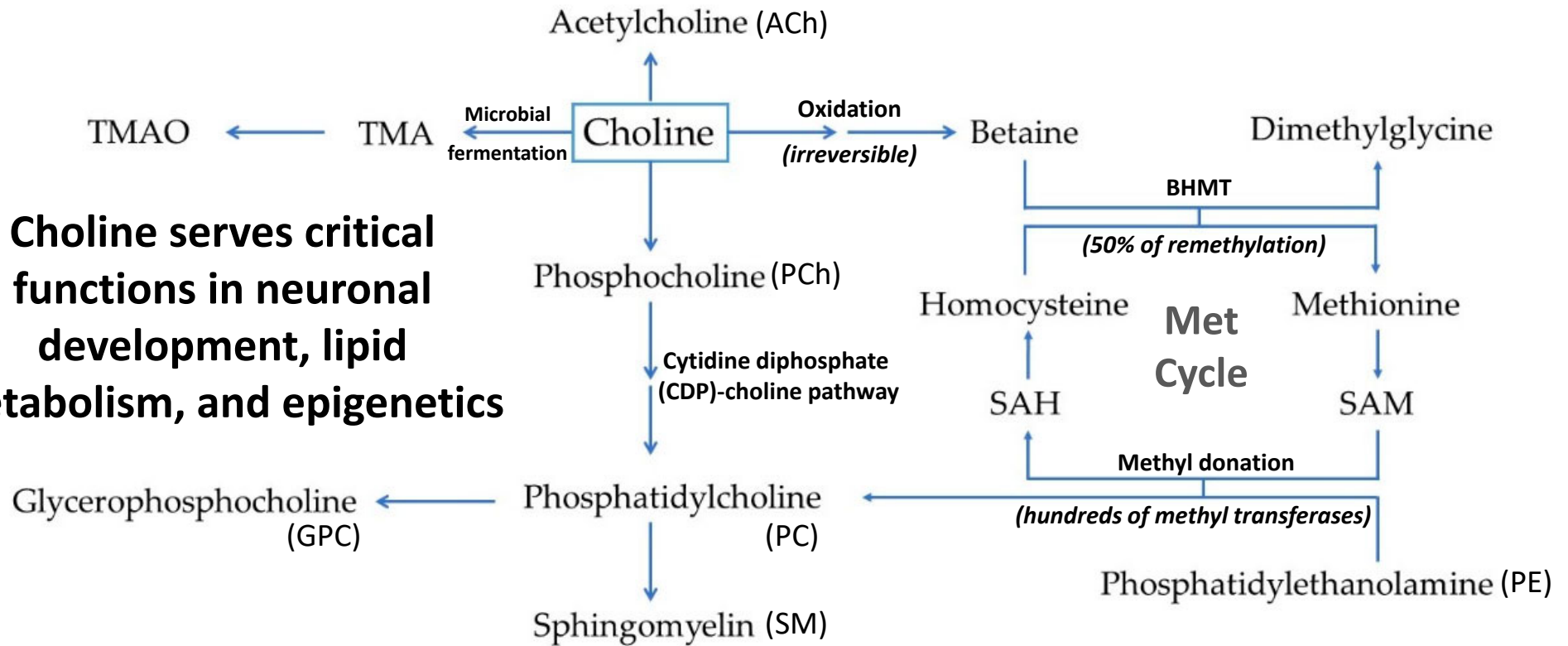
- Cellular maintenance and growth across all life-stages
 - Neurotransmission (sphingomyelin, acetylcholine)
 - Membrane synthesis (component of phospholipids, especially PC)
 - Lipid transport (lipoprotein synthesis)
 - One-carbon metabolism (betaine)



Choline Metabolism



Choline serves critical functions in neuronal development, lipid metabolism, and epigenetics



Abbreviations: SAM, S-adenosylmethionine; SAH, S-adenosylhomocysteine; TMA, trimethylamine; TMAO, trimethylamine-N-oxide

Adapted from Wiedeman et al., 2018; *Nutrients* 10, 1513

- Dietary free choline is preferentially used for biosynthesis of acetylcholine (Ach) and phosphatidylcholine (PC)
- PC is most abundant choline form in the body
 - 70% of total hepatic PC synthesized via CDP-choline pathway
 - Less efficient synthesis from PE via 3 methyl-transfer reactions (PEMT)
- Radiolabel studies confirm that all choline forms are absorbed, but they differ in metabolic kinetics and end-products
 - Water-soluble forms are absorbed faster and elicit higher tissue incorporation rates compared with lipid-soluble forms

- Reduced growth and reproductive performance
- Hepatic lipid accumulation
- Tissue development abnormalities
 - Bone/cartilage formation, neural tube closure, cognitive function
 - Perosis (chondrodystrophy) in broiler chickens is the classic choline deficiency sign; may progress to slipped tendons

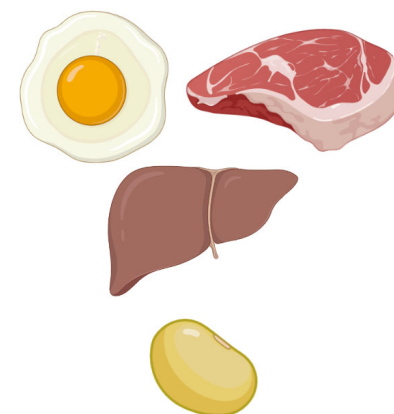


Photo credit to A. Marchioro and Wang et al., 2015

Dietary Sources of Choline

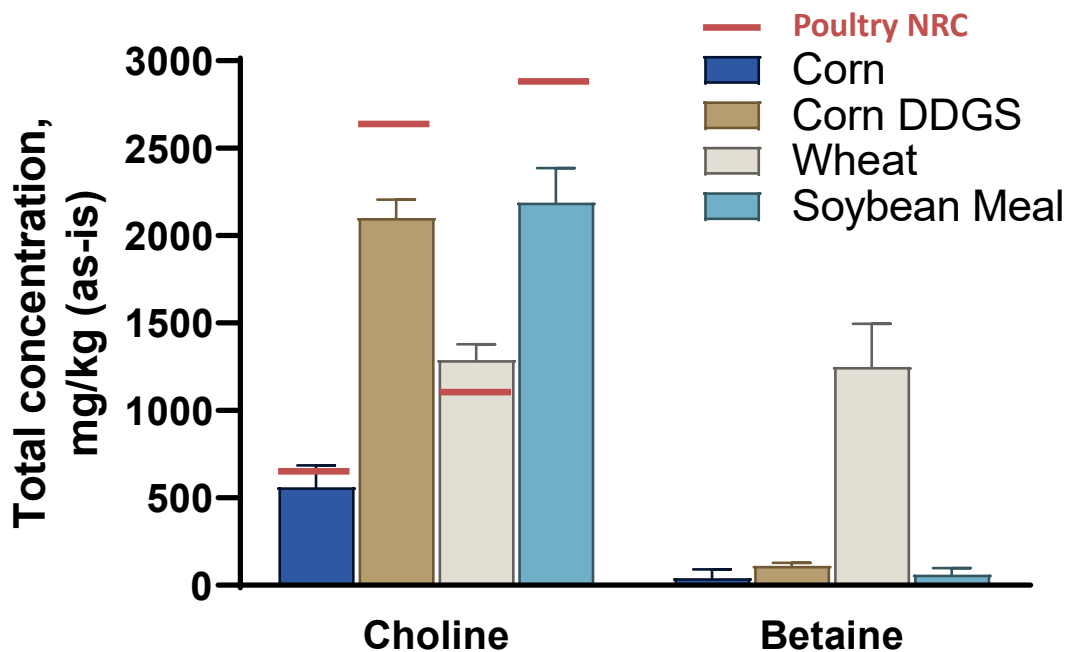


- Ingested form depends on species and physiological stage
- Animals transition from water-soluble forms (milk/egg yolk) to lipid-soluble forms (oilseed meals) with age
- Enriched sources are those of animal origin (eggs, meat, liver), but oilseed meals also contain (PC; aka lecithin)
- Bioavailability differs between choline sources and forms
- USDA maintains the most complete dataset of foods containing choline-related nutrients¹
- NANP Feed Composition database: animalnutrition.org



¹<https://www.ars.usda.gov/ARSUserFiles/80400525/data/choline/choln02.pdf>

Choline-containing Feedstuffs



- Variability in choline content of practical ingredients (CV range: 5-22%; *unpublished*)
- Virtually no betaine in feedstuffs apart from wheat

Commercial supplements

- Choline chloride
 - Dry (50-70% purity)
 - Liquid (70-75% purity)
- Choline bitartrate, citrate

Plant-based ingredients predominantly contain phosphatidylcholine (lipid-soluble form)

Relative Bioavailability (RBV)



- Few measures of bioavailability exist in the literature
- Broiler model using SPI-based diet containing 2-amino-2-methyl-1-propanol (inhibits *de novo* choline synthesis)



- RBV estimates

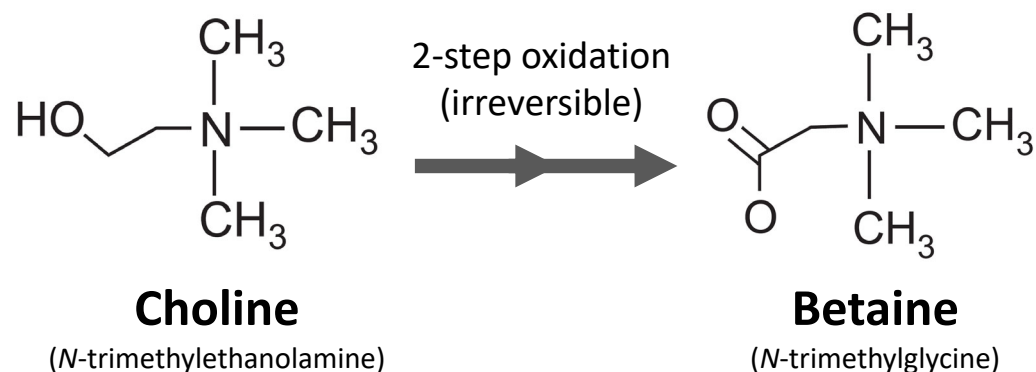
- Soybean meal: 77-90%
- Canola meal: 25-35%
- Peanut meal: 70-80%

Canola meal

- Analyzed total choline: > 6,000 mg/kg
- 3-times more total choline than SBM, but significantly lower available choline
- Likely related to sinapine (choline ester)

Feedstuff type and processing methods have profound influence on bioavailable choline content

- Choline provides labile methyl groups via betaine
- Betaine remethylates Hcy to Met, with SAM serving as the donor to hundreds of methyltransferase reactions



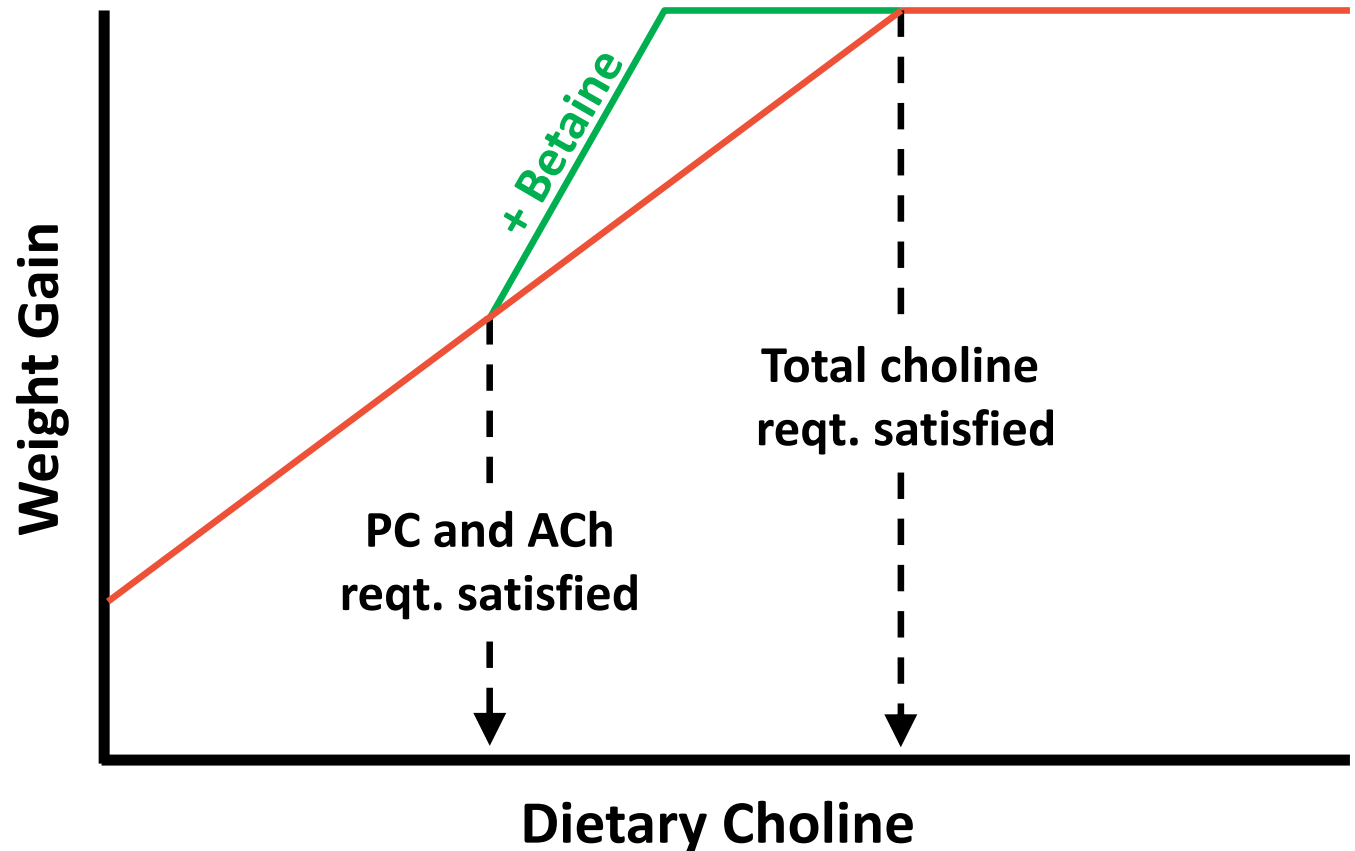
- Betaine does not contain choline (per se), which means exogenous betaine can only spare one function of choline: methyl donation
- Species-dependent metabolic considerations

Choline-sparing Effect of Betaine



Theory: First 2
functions of choline
will be satisfied at
50% of the total
choline requirement

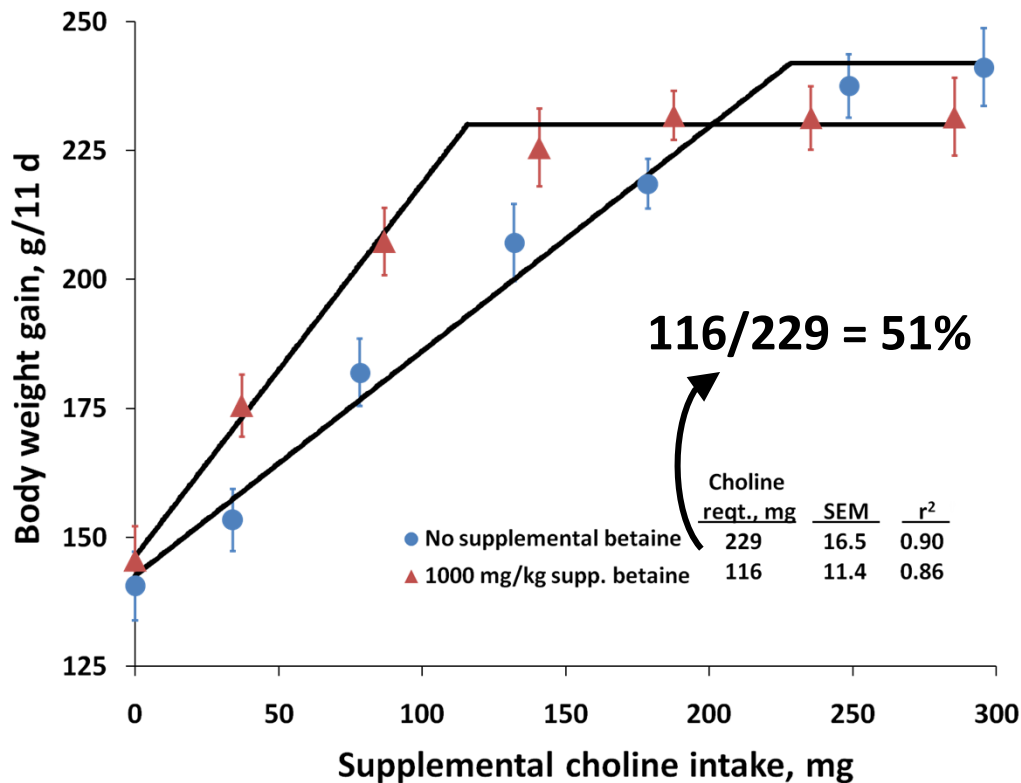
Predicted outcome:
No betaine response
until PC and ACh
functions satisfied



Choline-sparing Effect of Betaine

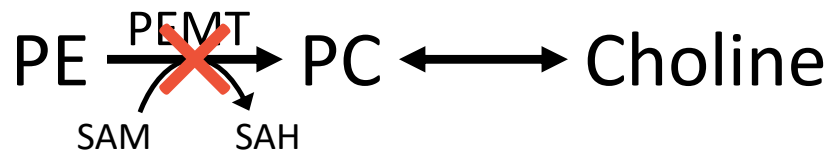


- Choline-free purified diet containing adequate methionine



- Betaine could NOT spare choline in a choline-free diet
- Preformed dietary choline is required to satisfy the ACh and PC functions (50% of total choline requirement)
- Betaine was able to satisfy the remaining 50% portion of the choline requirement specific to methyl donation

- Relatively high dietary requirement for preformed choline
 - Lacking in hepatic PEMT capacity, so *de novo* synthesis is low
 - Relatively high choline oxidase activity favors betaine formation
- Betaine serves as a potent osmolyte to counteract toxic effects of uric acid in the avian kidney
- Inadequate choline causes reduced growth due to fatty liver and incidence of perosis



Choline Requirements in Poultry



- Diets high in protein (but not Met alone) increase the dietary choline requirement, possibly through enhanced degradation
- PEMT activity increases with age; challenging to create a choline deficiency after birds are 8 weeks post-hatch
- Total choline requirements (Poultry NRC, 1994)
 - Broiler chickens: 750-1,300 mg/kg diet
 - Laying hens: 1,100-1,310 mg/kg diet
 - Turkeys: 800-1,600 mg/kg diet
 - Quail: 1,500-2,000 mg/kg diet



Choline Requirements in Pigs



- Lower dietary requirement compared with chickens due to efficient de novo choline synthesis
- Sufficient choline can be obtained via milk and practical diets
- No growth benefits in pigs consuming corn-SBM-based diets, where methionine can completely spare choline
- Total choline requirements (Swine NRC, 2012):
 - Starter/grower/finisher: 400-600 mg/kg diet
 - Gestation/lactation: 600-1,250 mg/kg diet



Johnson and James, 1948; Neumann et al., 1949; Lowry et al., 1987

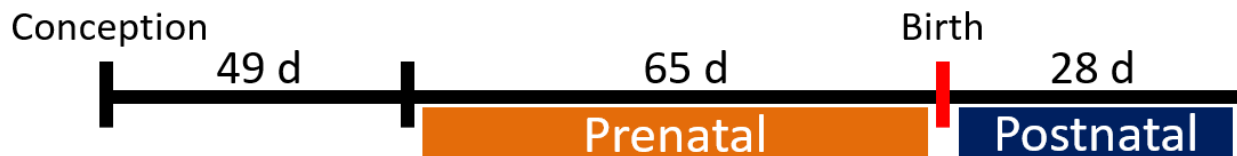
Choline in Sow Nutrition



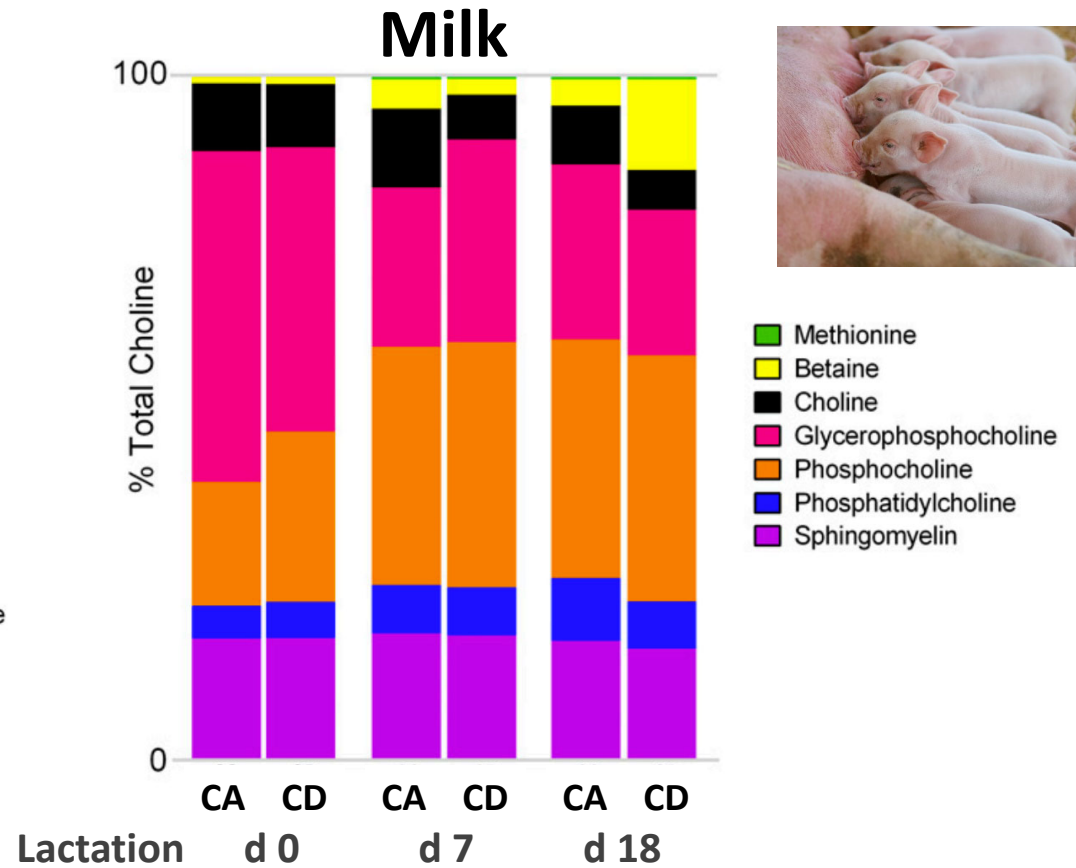
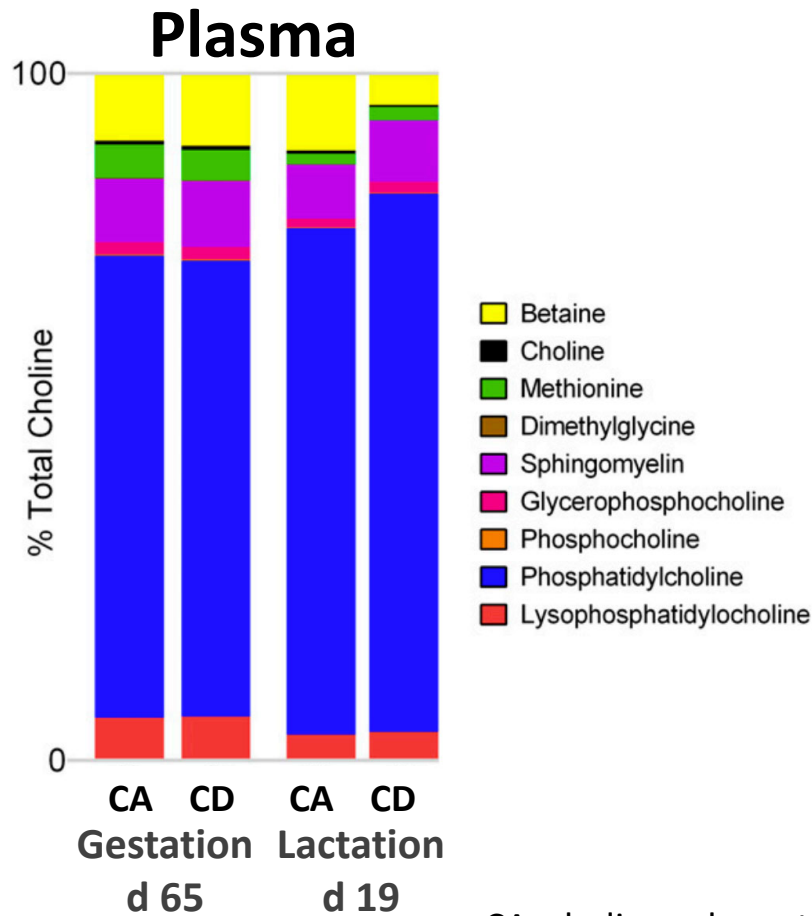
- Some evidence that higher choline may benefit reproductive performance of sows (Stockland and Blaylock, 1974)
 - Increased conception rate, increased total born alive
- Choline intake during gestation/lactation influences:
 - Sow’s milk composition (choline, amino acids, fatty acids)
 - Body choline concentrations and forms
 - Metabolomic profiles and brain development of pigs



Choline-adequate (**CA**)
 vs.
 Choline-deficient (**CD**)



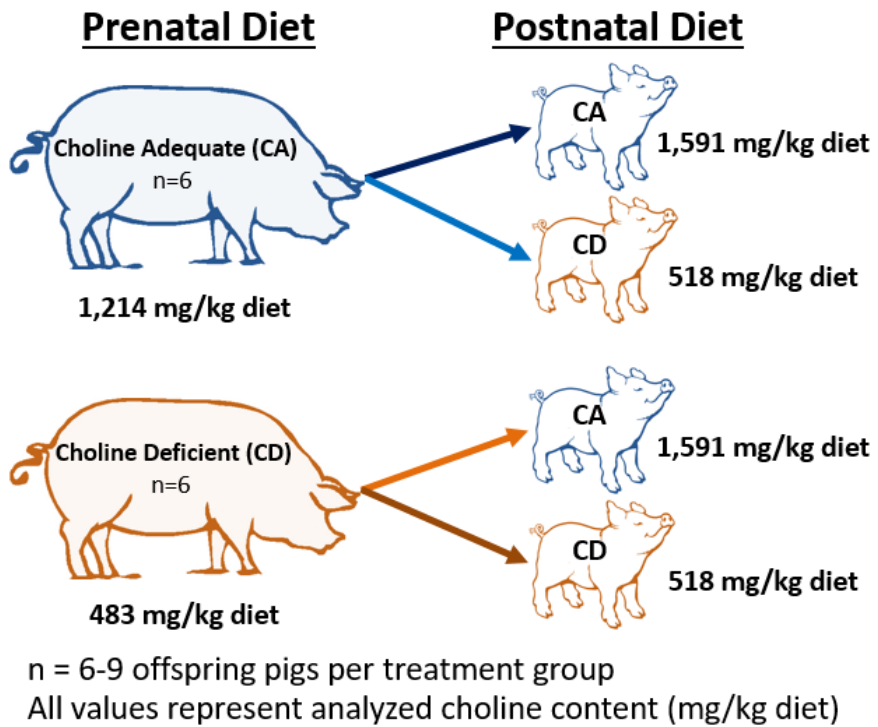
Perinatal Choline Status in Sows



CA, choline-adequate; CD, choline-deficient

Mudd et al., 2016; J. Nutr. 146, 2216

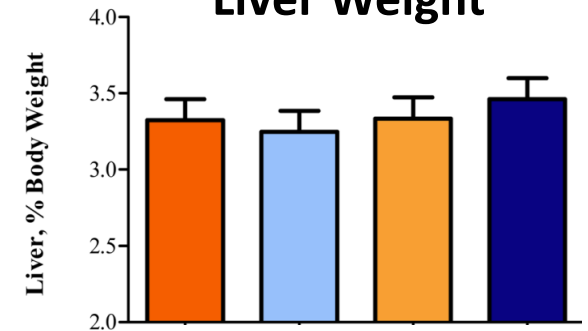
Perinatal Choline Status in Pigs



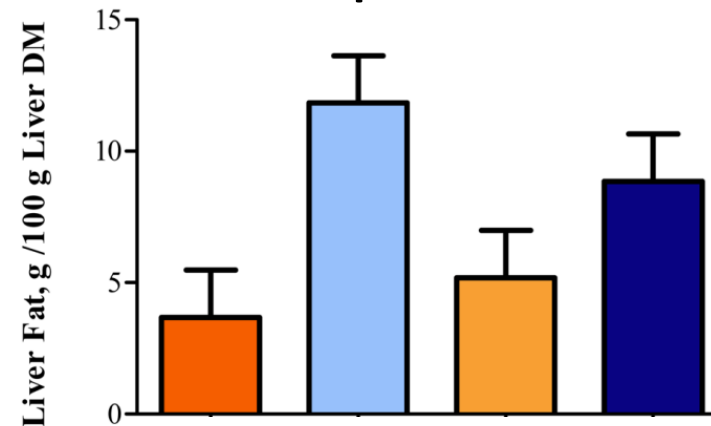
Prenatal / Postnatal

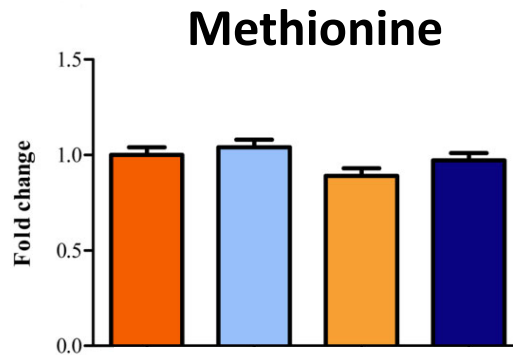
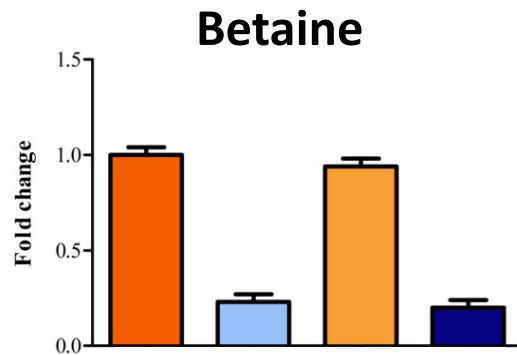
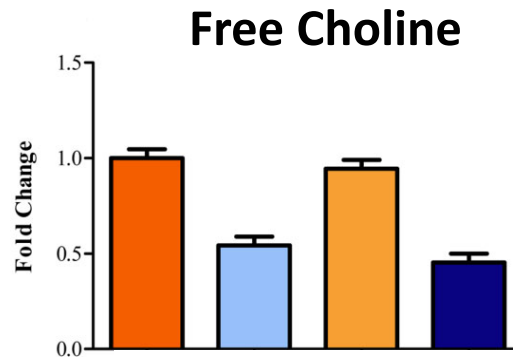
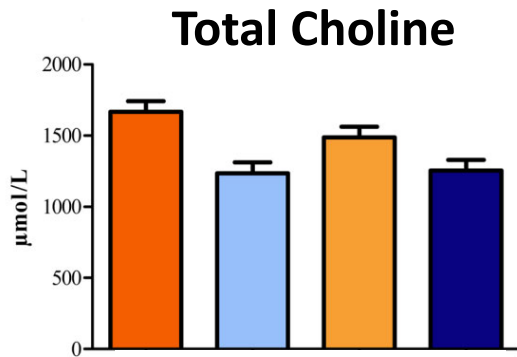
- Adequate / Adequate
- Adequate / Deficient
- Deficient / Adequate
- Deficient / Deficient

Liver Weight



Liver Lipid Content





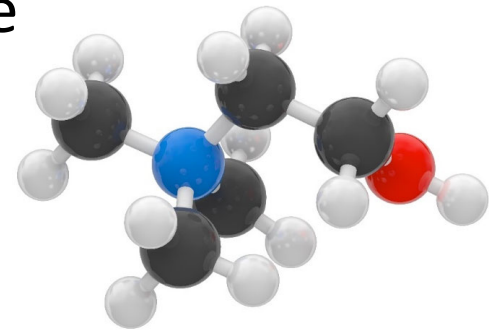
Prenatal / Postnatal

- Adequate / Adequate
- Adequate / Deficient
- Deficient / Adequate
- Deficient / Deficient



- Plasma metabolomics suggest stark changes to choline-related metabolites
- Amino acid, lipid, and carbohydrate metabolism altered
- Liver health biomarkers elevated in postnatal CD pigs

- Choline is a ‘pervasive’ nutrient due crucial metabolic roles
- Species-specific metabolic idiosyncrasies drive requirements
- Analytical data for choline-related compounds is lacking
- Bioavailability and metabolic kinetics vary by choline form
- Potential for choline deficiency remains a practical issue
- Betaine also important, but distinct from choline



Questions?



Ryan N. Dilger, PhD

rdilger2@illinois.edu

Ph: (217) 333-2006

<http://go.illinois.edu/RNDilgerLab>

