‘Maternal and Child Nutrition Fueling Baby’s Brain Development’

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Nutrition in brain development during the first 1000 days

1

Nutritional status among pregnant women

2

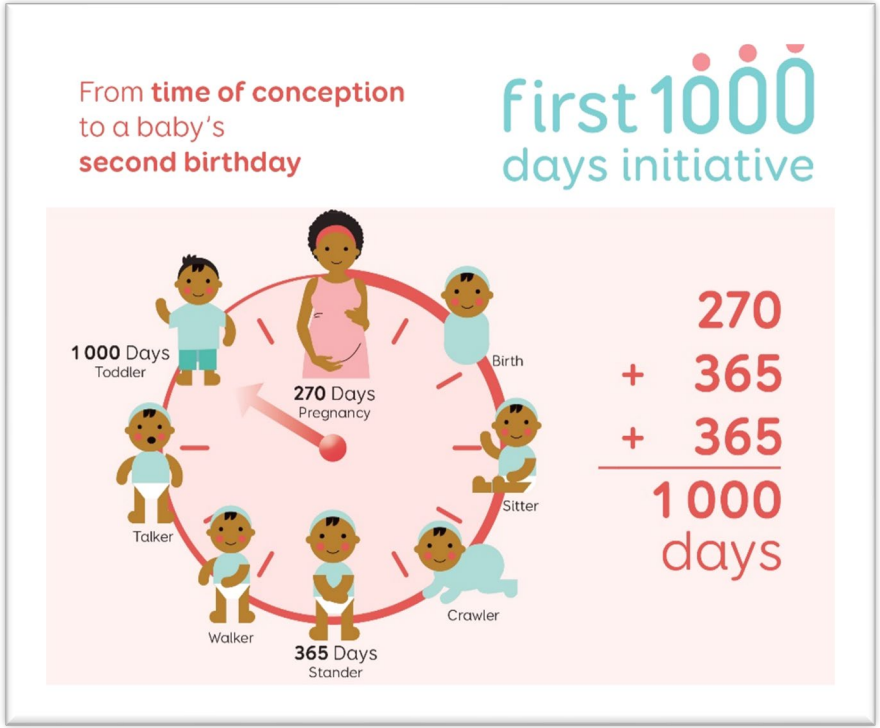
Nutrients in dairy and importance of dairy during pregnancy

3

Nutrition in brain development during the first 1000 days

1

1st 1000 days and brain development



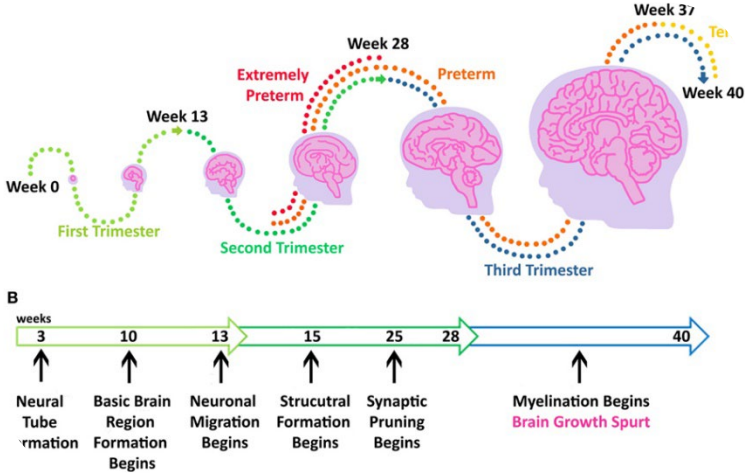
- **Unique** period of opportunity
- **Optimum** health and development
- **Grow**, **learn** and rise out of poverty

UNICEF, 2017

1st 1000 days and brain development

- All nutrients are important for **brain growth** and function

- Certain ones have **particularly significant** effects during **early** development



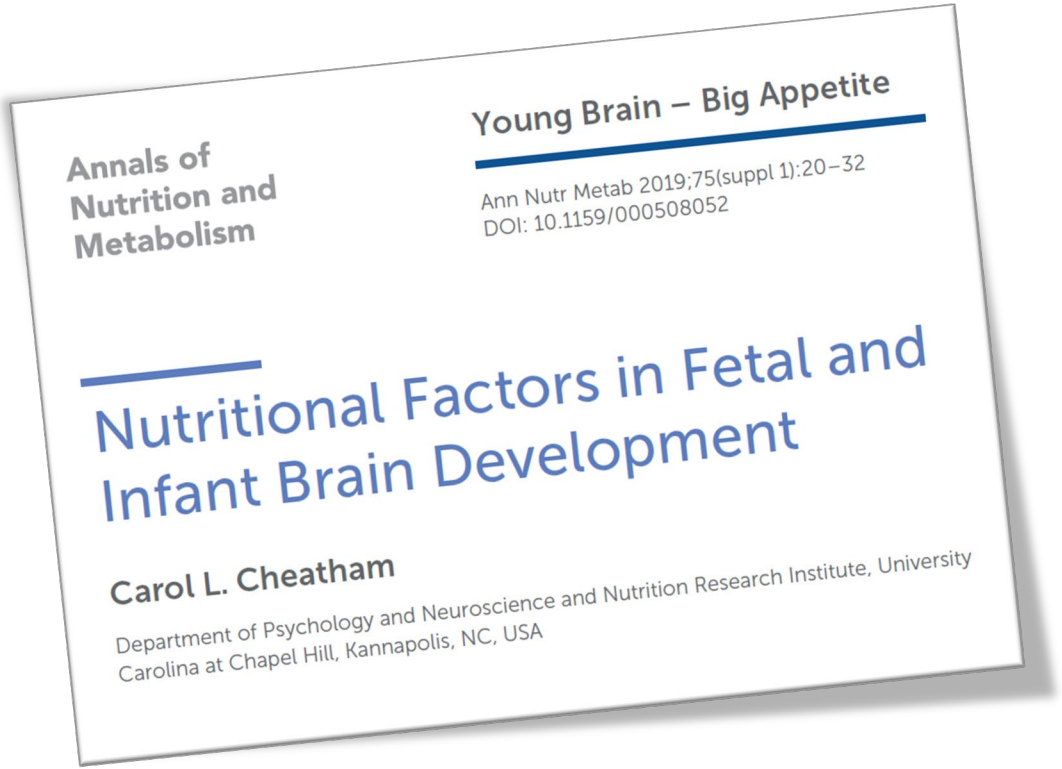
Cusick & Georgieff, 2016

1st 1000 days and brain development

Key nutrients for brain development are defined as those for which deficiency that is concurrent with **sensitive** or critical periods early in life results in **long-term dysfunction**

Cusick & Georgieff, 2016

1st 1000 days and brain development



Annals of Nutrition and Metabolism

Young Brain – Big Appetite

Ann Nutr Metab 2019;75(suppl 1):20–32
DOI: 10.1159/000508052

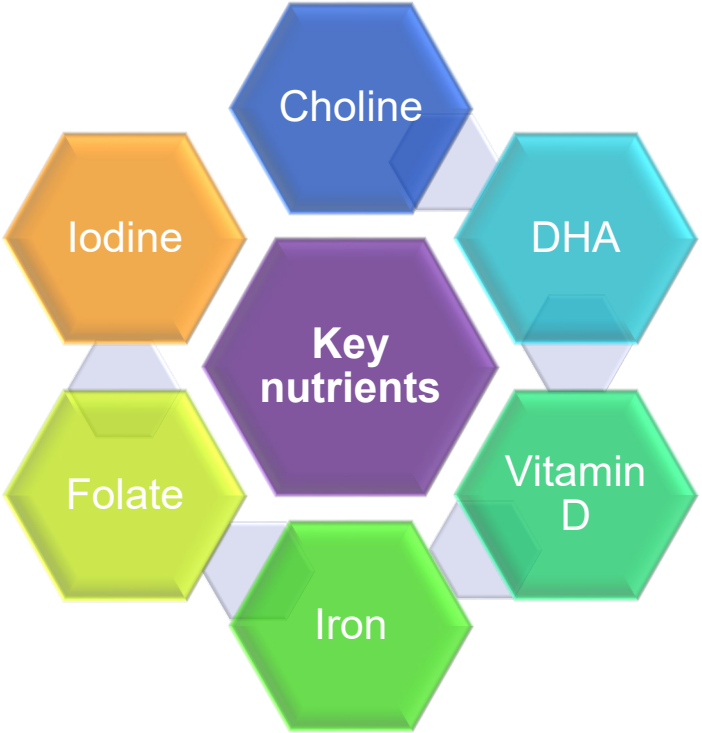
Nutritional Factors in Fetal and Infant Brain Development

Carol L. Cheatham

Department of Psychology and Neuroscience and Nutrition Research Institute, University Carolina at Chapel Hill, Kannapolis, NC, USA

Cheatham, 2020

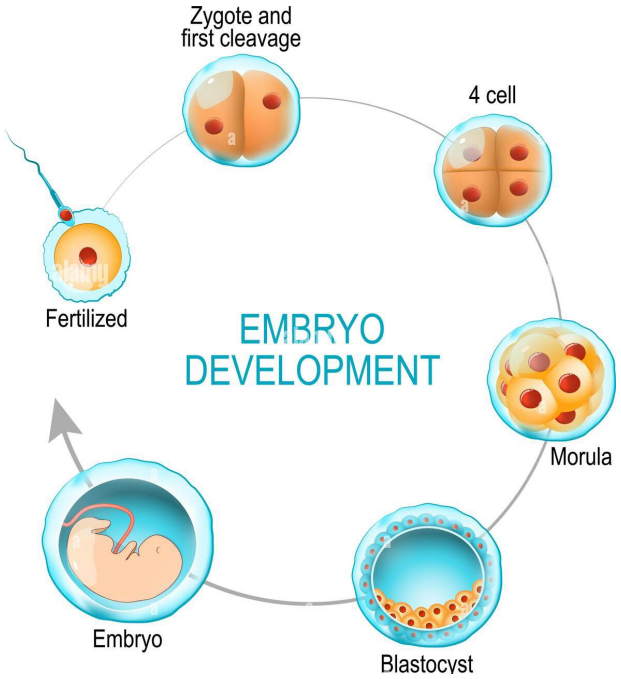
1st 1000 days and brain development



Cheatham, 2020

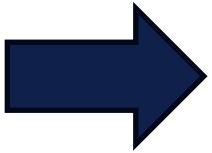
1st 1000 days - Preconception

In the first few weeks of gestation when **most women do not know that they are pregnant**, the zygote is growing at an incredible **rate**



Cheatham, 2020

1st 1000 days - Preconception

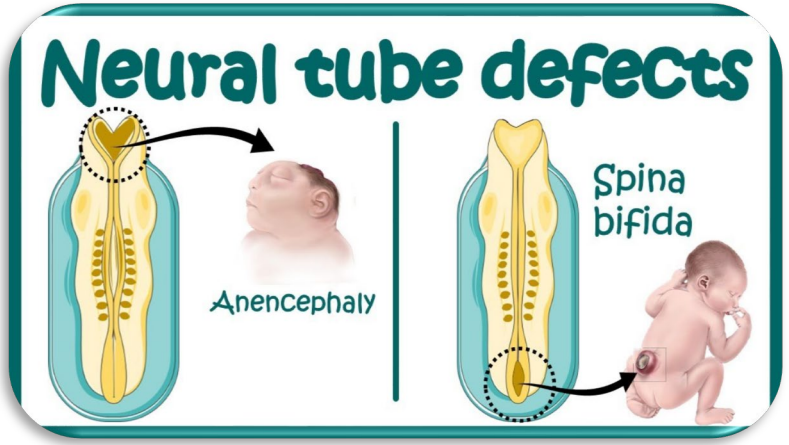


Preconception	Choline and metabolites Iodine
Prenatal	Vitamin D Iron Docosahexaenoic acid Choline
Postnatal	Iron Docosahexaenoic acid Choline

Cheatham, 2020

1st 1000 days – Folate

Neural tube closure occurs within the first **28 days** after **conception**, and defective closure is a neuro-ectodermal malformation - **neural tube defects** (NTDs)



Van Gool et al., 2018

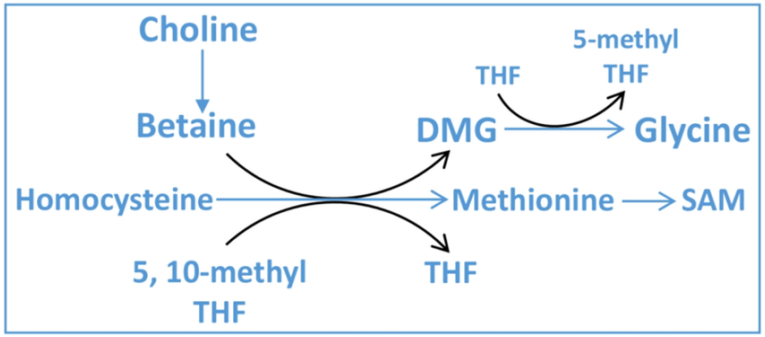
1st 1000 days – Folate

Exogenous folic acid probably **prevents** many **NTDs** by regulating **epigenetic** modifications (**methylation**) and/or cell **proliferation** (synthesis of purines), but the exact mechanisms are not completely **understood**

Van Gool et al., 2018

1st 1000 days – Folate

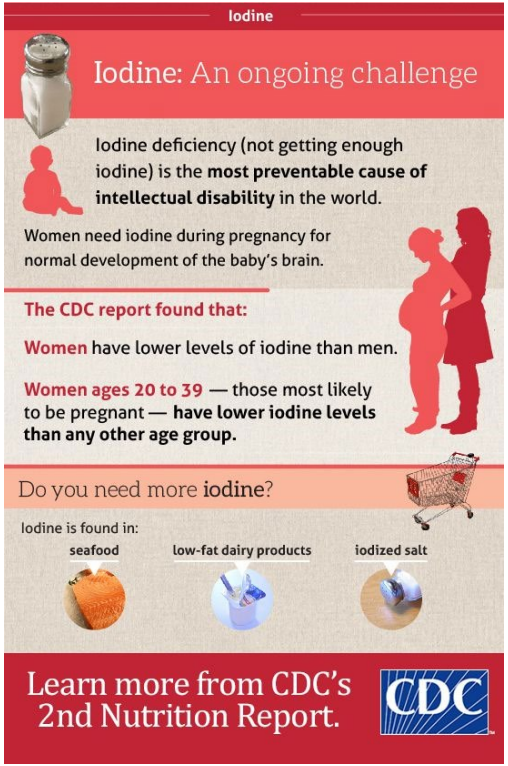
- **Folate** may **not** be the **primary** B-vitamin in the amelioration of NTDs
- Risk of NTDs is **furthest** reduced by a high intake of **methionine, choline,** and **betaine** in combination *rather* than intake of folate *alone*



Cheatham et al., 2018

1st 1000 days – Iodine

During pregnancy, **iodine** requirements increase → increased need for **thyroid hormones** (the fetal thyroid does not start working until the **second trimester**)



Cheatham et al., 2018

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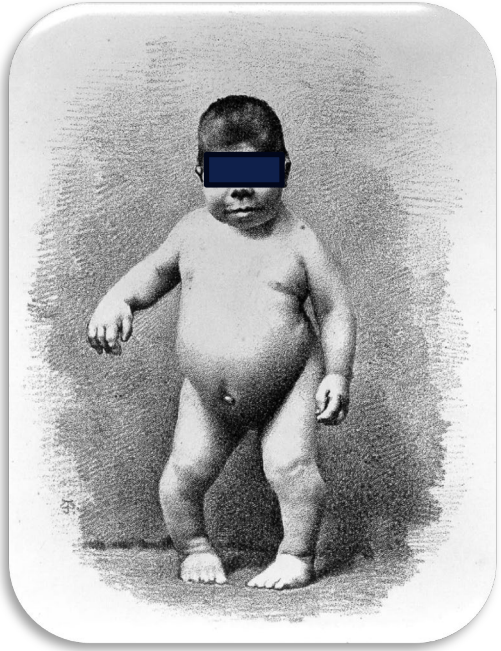
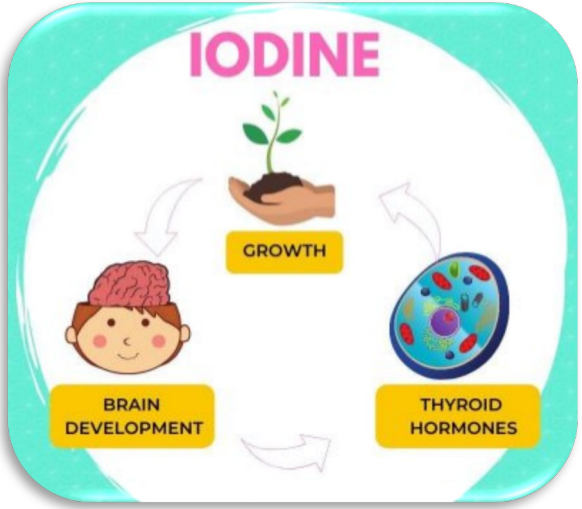
1st 1000 days – Iodine

If a woman is severely deficient in the first **few days or weeks of gestation**, the result is **cretinism** in the child, which is characterized by **mental deficiencies**, **deaf mutism**, and **motor spasms** of the arms and legs



Cheatham et al., 2018

1st 1000 days – Iodine



Because **thyroid hormones** are involved in **neurogenesis** and **neuronal migration** as well as several other neuronal processes, the effects of iodine deficiency can be **globally pervasive** in the **brain**

Cheatham et al., 2018

1st 1000 days – Iodine

- Even in the **absence** of **overt cretinism** → chronic iodine deficiency **negatively** affects **intelligence**
- A meta-analysis showed a **13.5 IQ** point difference between **individuals** living in **iodine-sufficient** and **iodine-deficient** areas

Prado & Dewey, 2014

1st 1000 days – Iodine

Recently, some (inconsistent) evidence showed that **offspring** of **mothers** with **low serum thyroid hormone** concentrations during **early pregnancy** might present an increased risk of **ADHD**

Metei & Pietrobelli, 2019

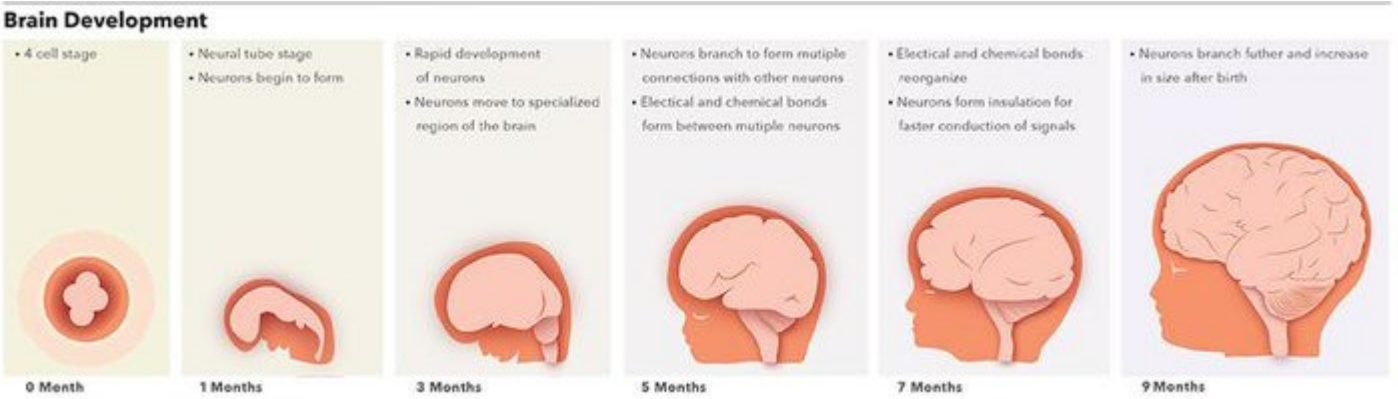
1st 1000 days – Iodine

- Additionally, Román et al. (2013) found a **consistent association** between **severe**, **early** gestation, **maternal hypothyroxinemia** and **autistic** symptoms in offspring

- The possibility of preventive interventions must be further **investigated**

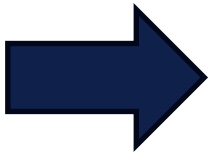
1st 1000 days - Prenatal

Fetal neural development is dependent on the nutritional environment **in utero**



Cheatham, 2020

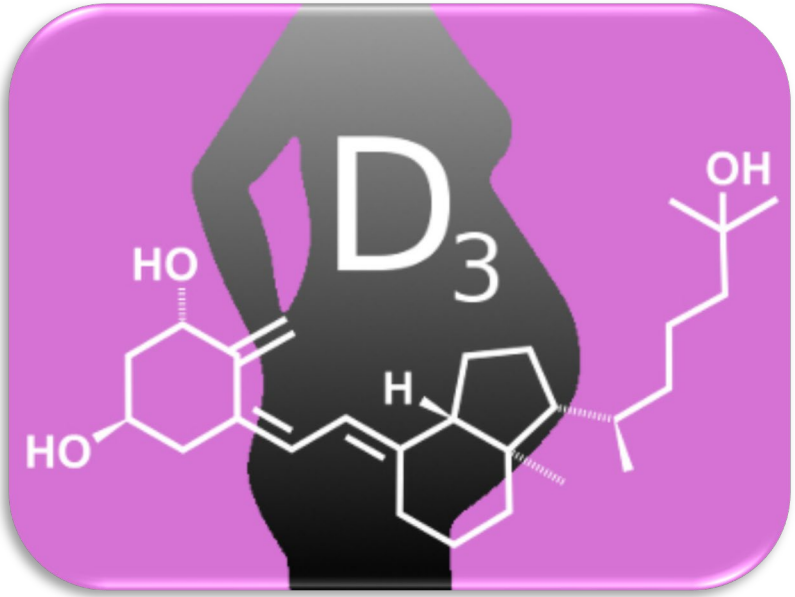
1st 1000 days - Prenatal



Preconception	Choline and metabolites Iodine
Prenatal	Vitamin D Iron Docosahexaenoic acid Choline
Postnatal	Iron Docosahexaenoic acid Choline

1st 1000 days – Vitamin D

- The **fetus** is wholly **dependent** on maternal provision of vitamin D
- When the **mother** is deficient, the fetus is **deficient**



1st 1000 days – Vitamin D

- Animal models → vitamin D deficiency results in **morphologically different brains** in the offspring: vitamin D has a role in **brain size**, **ventricle size**, **cell proliferation**, and **growth factor signaling**

- **Human** trials?

Cheatham, 2020

1st 1000 days – Iron

Pregnancy increases maternal iron demand for 3 reasons:

- **Maternal plasma and blood volumes** are increased during pregnancy
- In addition, the **fetus** requires iron for its **own metabolic** and **oxygen** delivery needs as well as the **loading** of its comparatively large endogenous iron **stores** that will be used in the first **6 months** of postnatal life
- The **placenta** is a highly metabolically **active** organ with large iron requirements

Georgieff, 2020

1st 1000 days – Iron

Fetal **iron sufficiency supports neural energy metabolism**, the development of **dendrites** and **synapses**, the synthesis of **neurotransmitters**, and the onset of **myelination**

Cheatham, 2020

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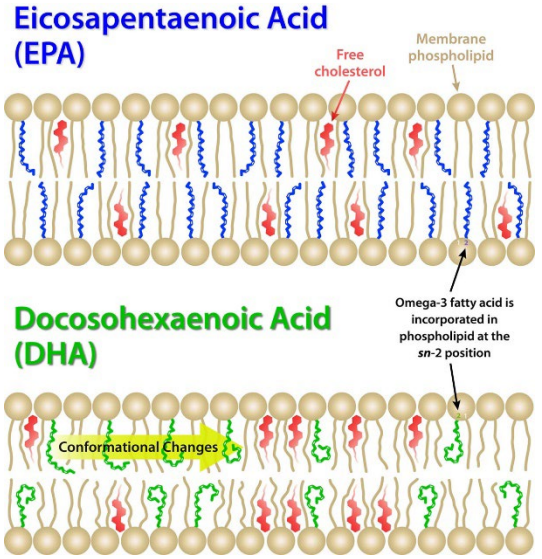
1st 1000 days – Iron

When a **fetus is iron deficient** for extended periods of time, **brain development** does **not** proceed on a **typical** trajectory and the suboptimal outcomes are most likely **irreversible** even when iron is replete

1st 1000 days – DHA

- DHA is integral to **cellular** and **neural** function as it and other fatty acids comprise the **phospholipid bilayer**
- The demand is highest in the **3rd trimester**, and multiple maternal **pathways** are **upregulated** to insure sufficient supply



1st 1000 days – DHA

- Whether there are any effects of **maternal supplementation** with fatty acids on infant **cognition** has been called into **question** by systematic reviews
- Study **design**, background **diet**, and background **genetics** are integral in the consideration of the effects of fatty acids on cognition

1st 1000 days – Choline

The **American Academy of Pediatrics** (AAP) lists **choline** as a **key** nutrient that supports **neurodevelopment** and that deficiencies thereof can likely to lead to **long-term deficits in cognitive functioning**

American Academy of Pediatrics

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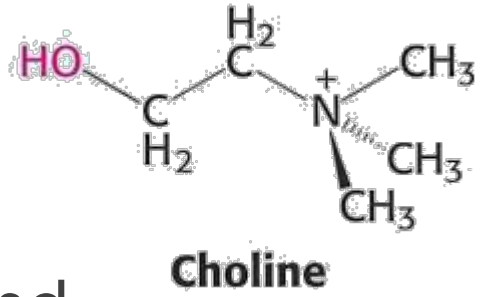
AAP, 2018

1st 1000 days – Choline

- The foetus requires high levels of **phospholipids**, such as **phosphatidylcholine** and **sphingomyelin**, which are both derived from **choline**



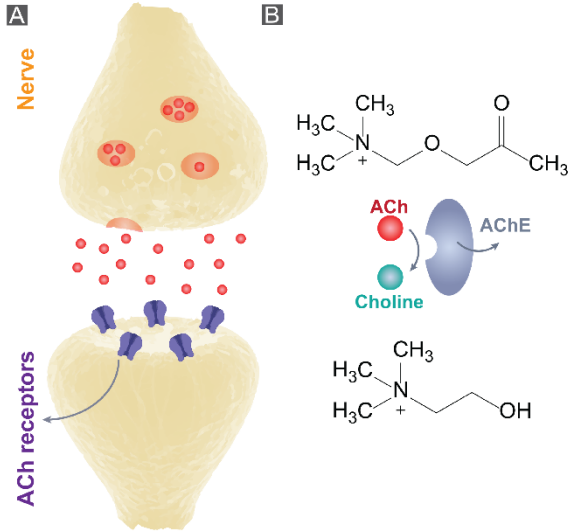
Choline

- These phospholipids are involved in **rapid cell division**, **growth** of tissues and **myelination** of **nerves**

1st 1000 days – Choline

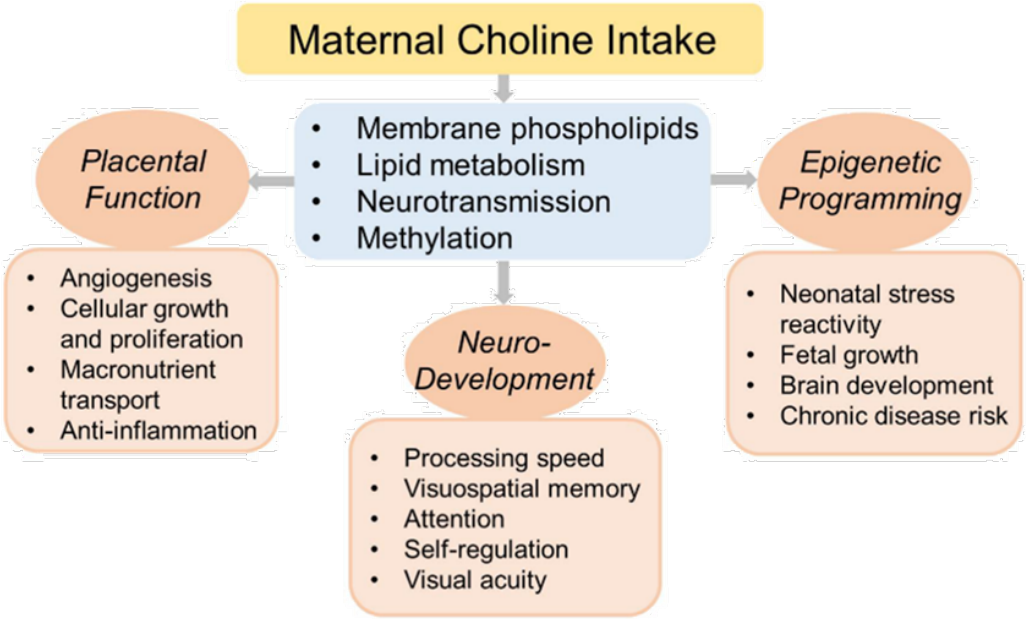
- **ACh** affects numerous processes in the foetal brain (**neurogenesis**, progenitor cell **proliferation** and **synaptic plasticity**)

- **ACh** → development of the **hippocampus**, which influences memory, attention and learning



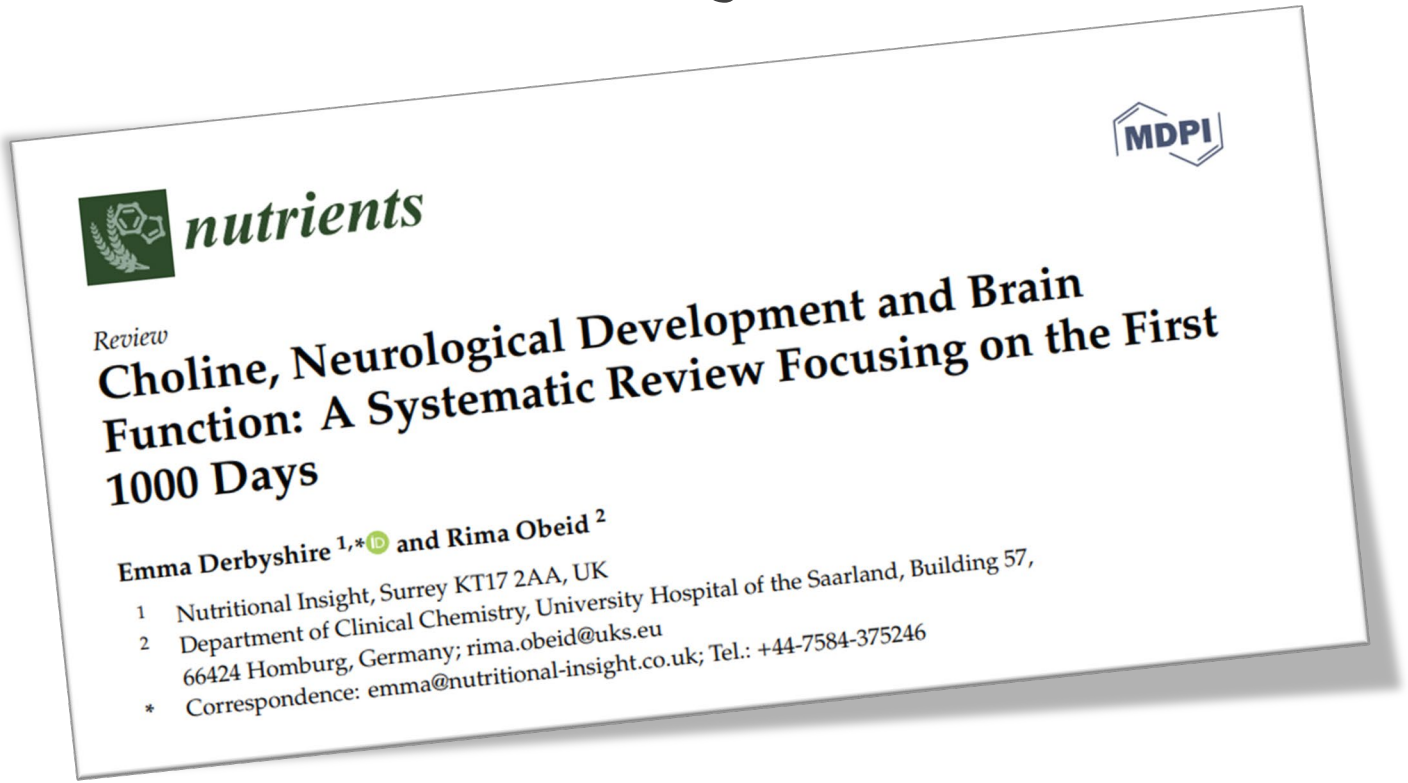
1st 1000 days - Choline

During pregnancy, various **metabolic and physiologic processes** are influenced by maternal **choline** intake:



Korsmo & Jiang, 2019

1st 1000 days - Choline



MDPI

nutrients

Review

Choline, Neurological Development and Brain Function: A Systematic Review Focusing on the First 1000 Days

Emma Derbyshire [1,*] and Rima Obeid [2]

1 Nutritional Insight, Surrey KT17 2AA, UK
2 Department of Clinical Chemistry, University Hospital of the Saarland, Building 57, 66424 Homburg, Germany; rima.obeid@uks.eu
* Correspondence: emma@nutritional-insight.co.uk; Tel.: +44-7584-375246

Derbyshire & Obeid, 2020

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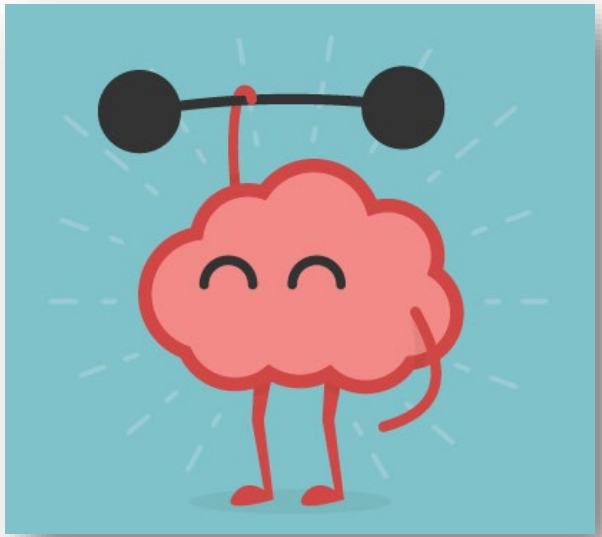
1st 1000 days – Choline

Evidence from **animal models** shows that **higher choline intakes during pregnancy**, and in early **postnatal** development, can **protect** the **brain** from the **neurological damage** associated with **fetal alcohol syndrome** and inherited conditions such as **Down Syndrome**

1st 1000 days – Choline

It also has **lasting effects in adulthood**, including **improved cognitive function**, **prevention** of age-related **memory decline**, and **neurological** changes linked to conditions such as Alzheimer's disease

1st 1000 days – Choline



Evidence from a growing body of human studies also shows that **choline interventions** in **pregnancy** can improve **infant processing speed** and visuospatial **memory** in childhood

Derbyshire & Obeid, 2020

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1st 1000 days – Choline

From the evidence-base, it is increasingly apparent that **choline** can **attenuate** some of the **neurological damage** associated with **alcohol exposure** during pregnancy

Derbyshire & Obeid, 2020

1st 1000 days - Choline

Association between Maternal Choline, Fetal Brain Development, and Child Neurocognition: Systematic Review and Meta-Analysis of Human Studies

Rima Obeid,[1] Emma Derbyshire,[2] and Christiane Schön[3]

[1] Department of Clinical Chemistry and Laboratory Medicine, University Hospital of the Saarland, Homburg, Germany; [2] Nutritional Insight, Surrey, United Kingdom; and [3] BioTeSys GmbH, Esslingen, Germany

Obeid et al., 2022

1st 1000 days – Choline

Low maternal choline intake/circulating serum total **choline** in early pregnancy was associated with a **36% higher OR for NTDs**

Obeid et al., 2022

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1st 1000 days – Choline

In general, **RCTs** providing up to **1 g choline/d** to **pregnant** women showed **favorable** effects on certain **neurocognitive** domains of the **child**

Obeid et al., 2022

1st 1000 days – Choline

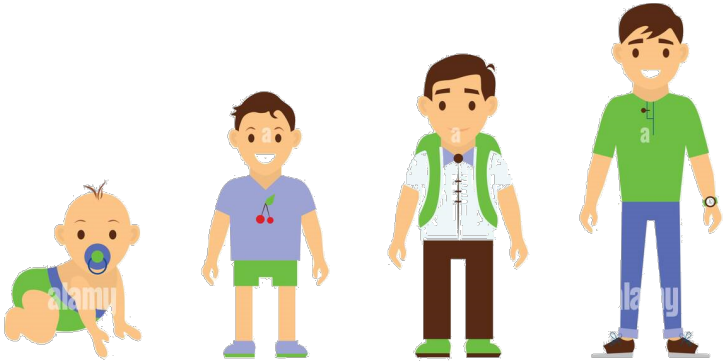
Choline intake exceeding current recommendations appears to be **necessary** to influence child neurocognition

Obeid et al., 2022

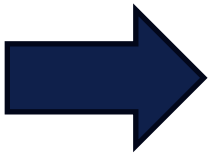
1st 1000 days – Postnatal

- Brain development continues into the **second decade** of life

- Postnatally, the brain is most **rapidly developing** and most **plastic** during **infancy and toddlerhood**



1st 1000 days – Postnatal



Preconception	Choline and metabolites Iodine
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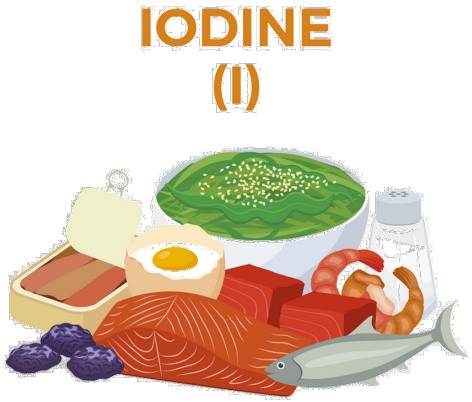
Cheatham, 2020

Nutritional status among pregnant women

2

Nutritional status of pregnant women



Nutritional status of pregnant women

- Globally, **40% of children** aged 6–59 months, **37% of pregnant** women and **30% of WRA** are affected by **anaemia**

- **Iron deficiency** is considered the most **common** nutritional deficiency leading to anaemia

WHO, 2023

Nutritional status of pregnant women

- Presently, approximately **90%** of **Americans** have **choline** intakes falling **below the basic AI**, including most **pregnant** and breastfeeding mothers (AI of 450 and 550 mg/day, respectively)
- We found **similar** results in **SA** in BFN

Ronto et al., 2018; Robb et al, 2021

Nutritional status of pregnant women

Iodine is one of the most **common** nutrient **deficiencies** and is estimated to affect **35–45%** of the world's population

Hatch-McChesney & Lieberman, 2022

Nutrients in dairy and importance of dairy during pregnancy

3

Dairy and neurodevelopment

- Choline
- Iodine
- Folate
- Protein
- Riboflavin
- Calcium
- Magnesium
- Vitamin B12

Dairy and neurodevelopment – Choline

- **Epidemiological** studies have suggested that there are only **10 major sources** of choline in the diet, which include **dairy**

Richard et al., 2016

Food	Choline (mg) / 100g	Serving size	Choline (mg)
Eggs			
Eggs, whole	250.0	1 large	146.9
Eggs, white	1.1	1 large	0.4
Eggs, yolk	680.0	1 large	139.4
Fish			
Atlantic cod	84.0	90 g	71.1
Pink salmon	91.0	90 g	81.9
Tuna, drained, in water	29.0	90 g	26.1
Meats			
Beef chuck	100.0	90 g	90.0
Beef liver	420.0	90 g	362.1
Pork loin	78.0	90 g	66.7
Chicken, dark meat	84.0	90 g	75.6
Chicken, light meat	62.0	90 g	55.8
Chicken liver	290.0	90 g	277.8
Dairy			
Milk, whole	14.0	250 ml	34.9
Milk, skim	16.0	250 ml	39.2
Cheese, cheddar	17.0	45 g	7.7
Yoghurt, low-fat	15.0	100 g	15.0
Other			
Soybeans, matured	120.0	30 g	34.9
Peanuts, dry roasted	53.0	30 g	15.9
Mushrooms, white	17.0	125 ml	15.9
Broccoli, cooked	40.0	125 ml	31.3
Bread, white	15.0	40g	6.0
Bread, whole wheat	27.0	40g	10.8

Patterson et al., 2008

Dairy and neurodevelopment – Choline

Women (Canada) who reported consuming ≥ **500 ml** of milk in day were **2.8** times more likely to meet daily choline intake recommendations compared with those **consuming < 250 ml** of milk/d during pregnancy

Lewis et al., 2014

Dairy and neurodevelopment - Choline

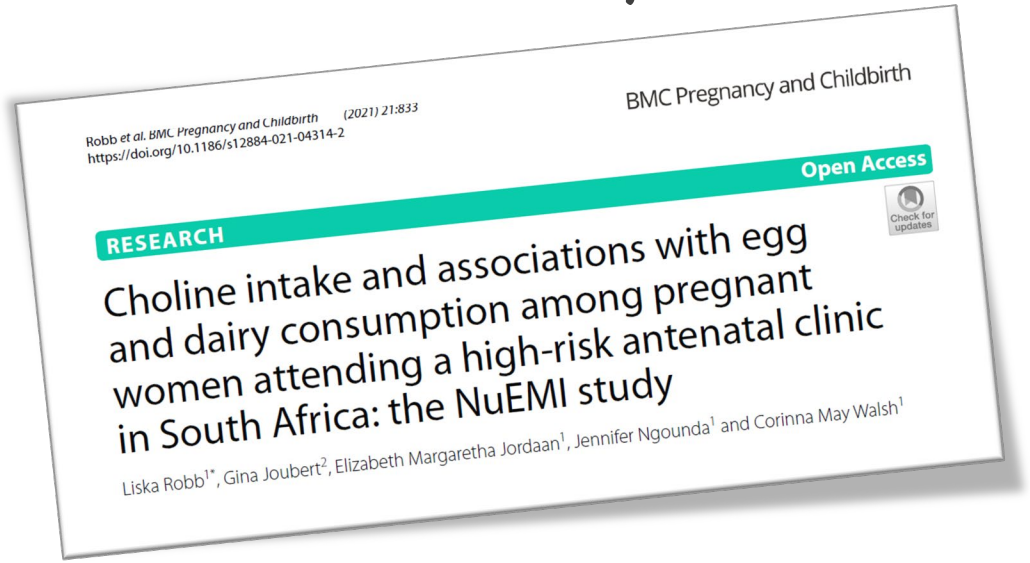
Choline intake during pregnancy and lactation

Table 3. Most commonly reported food categories* contributing to total dietary choline intake during pregnancy and lactation in the APrON (Alberta Pregnancy Outcomes and Nutrition) cohort

	Pregnancy		Lactation	
Ranks	Food category*	Contribution (%)†	Food category*	Contribution (%)†
1	Dairy	20·9	Dairy	16·9
2	Eggs	12·4	Meat	15·0
3	Meat	11·1	Eggs	13·8
4	Poultry	8·9	Vegetables	8·3
5	Vegetables	8·5	Poultry	8·2
6	Baked products	7·7	Baked products	7·2
7	Fruits	6·6	Fruits	4·8
8	Legumes	4·1	Legumes	3·5
9	Finfish and shellfish	2·7	Finfish and shellfish	3·2
10	Mixed dishes	2·6	Fast foods	3·1
Sum‡		85·4		84·0

Lewis et al., 2014

Dairy and neurodevelopment – Choline



Robb et al. BMC Pregnancy and Childbirth (2021) 21:833
https://doi.org/10.1186/s12884-021-04314-2

BMC Pregnancy and Childbirth

Open Access

RESEARCH

Choline intake and associations with egg and dairy consumption among pregnant women attending a high-risk antenatal clinic in South Africa: the NuEMI study

Liska Robb[1*], Gina Joubert[2], Elizabeth Margaretha Jordaan[1], Jennifer Ngounda[1] and Corinna May Walsh[1]

Pregnant women (central SA) – full cream **cow's milk** was **main choline** food **item** contributor

Robb et al., 2021

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Dairy and neurodevelopment – Choline

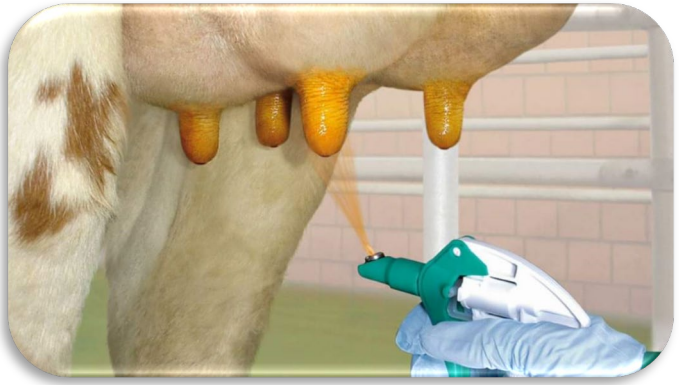
Table 6 Weekly egg and daily dairy intake associated with inadequate choline intake: logistic regression

Variable	Description	Odds ratio (95% CI)	*p*-value
Weekly egg intake	none vs ≥ 5	49.78 (18.96; 130.68)	**< 0.0001**
	< 1 vs ≥ 5	21.82 (6.47; 73.62)	
	1 to < 3 vs ≥ 5	10.64 (5.23; 21.64)	
	3 to < 5 vs ≥ 5	3.30 (1.82; 5.98)	
Daily dairy intake	< 250 g vs ≥ 250 g	2.80 (1.64; 4.73)	**0.0002**

Robb et al., 2021

Dairy and neurodevelopment – Iodine

Cow's milk has a **naturally low iodine** concentration but is a **rich** source of **iodine** through **standard farming practices** such as the addition of **iodine salts** to cattle feed and use of **iodine- based disinfectants**



Witard et al., 2022

Dairy and neurodevelopment – Iodine

Milk and dairy products have been shown to be **determinants of iodine status** in **pregnant women** and young children

Witard et al., 2022

Dairy and neurodevelopment – Folate

Milk - and especially **fermented** dairy products like **yogurt**, **buttermilk** and different varieties of **cheeses** - are already recognised as **good** dietary sources of folates

Forssen et al., 2013

Dairy and neurodevelopment – Folate

Cifelli et al. (2022) → intake of **total dairy** and its **individual components**' was associated with **improved status and reduced risk** of **inadequacy** of **folate**

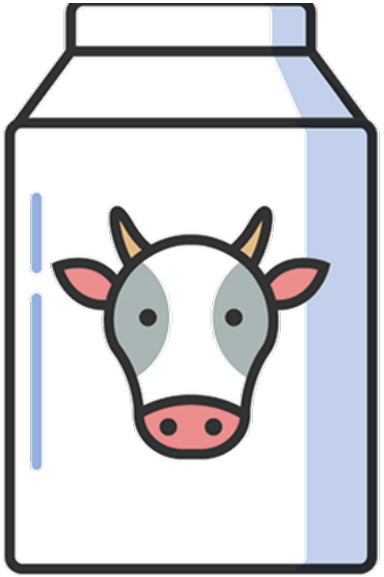
Dairy and neurodevelopment - Protein

Bovine milk protein is considered a **high quality**, or complete protein, because it contains all 9 of the **essential amino acids** in proportions resembling amino acid requirements

Davoodi et al., 2016

Dairy and neurodevelopment - Protein

Total **protein** content of bovine milk is approximately **3.5% by weight** (36 g/L)



Davoodi et al., 2016

Dairy and neurodevelopment – Protein

- Animal studies have shown that **maternal protein restriction** during **pregnancy** and **lactation** causes **abnormal brain development** among offspring

- **Maternal protein restriction** after implantation causes **epigenetic abnormalities** in the brain, and **behavioral abnormalities** among offspring

Miyake et al., 2023

Dairy and neurodevelopment – Riboflavin

- **Insufficiency** is linked to:
  - **Impaired thyroid** hormone regulation
  - **Low iron absorption**
  - **Poor brain lipid** metabolism

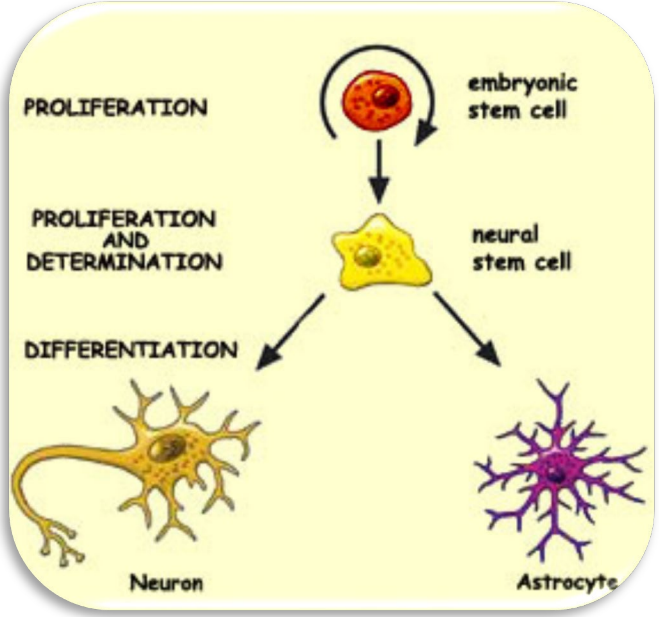
  → **adverse** effect on **fetal brain** function

Dairy and neurodevelopment – Calcium

- Required for the **influx** of **cellular excitation** via **Ca channels**
- This **facilitates neurotransmitter transport** and plays a role in **gene expression**, membrane **excitability** and **neuronal** development

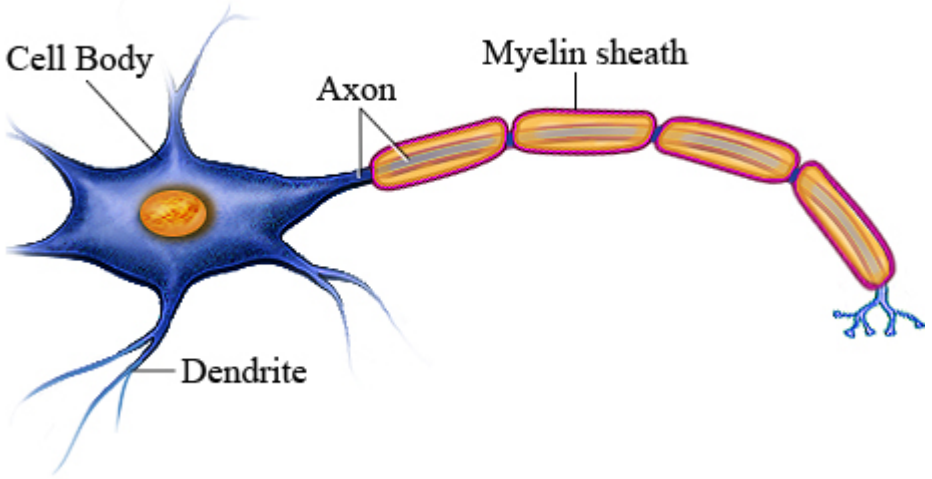
Dairy and neurodevelopment – Calcium

Also involved in **neuronal differentiation** by directly **controlling** the **neurotransmitter phenotype**, **dendritic** shape, and **neuronal axon** growth



Dairy and neurodevelopment – Cyanocobalamin

- Crucial for the **formation** of **myelin** in the **developing** fetal **brain** tissue
- **Nerve development** and cognitive processes depend on this **myelination**



Thank you!

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