

# Could we be overlooking a potential choline crisis in the United Kingdom?

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## INTRODUCTION

Choline can be likened to omega-3 fatty acids in that it is an ‘essential’ nutrient that cannot be produced by the body in amounts needed for human requirements. The United States (US) Institute of Medicine (IOM)<sup>1</sup> and European Food Safety Authority (EFSA)<sup>2</sup> recognise that choline plays an important role in the human body and have established dietary reference values. The American Medical Association<sup>3</sup> in 2017 published new advice stating that prenatal vitamin supplements should contain “evidenced-based” amounts of choline. Similarly the American Academy of Paediatrics<sup>4,5</sup> (from 2018) called on paediatricians to move beyond simply recommending a “good diet” and to make sure that pregnant women and young children have access to food that provides adequate amounts of “brain-building” nutrients with choline being listed as one of these. Unfortunately, in the UK choline is not yet included in food composition databases, main nutrition surveys nor official recommendations. The present article discusses the current choline situation and explains why more needs to be done to include and monitor this essential nutrient in the UK.

## About choline

Choline is an ‘essential’ nutrient for humans; and similar to omega-3 fatty acids, as the amount produced endogenously (in the liver) is not sufficient to meet human requirements,<sup>6</sup> it therefore needs to be obtained from dietary and supplement sources. Physiologically, choline is critical for a number of functions across the life cycle which include wide-ranging roles in human metabolism from neurotransmitter synthesis to cell structure and methylation, with choline deficiency being linked to liver disease, offspring cognitive function and potential neurological disorders.<sup>7,8</sup>

Functionally choline in its oxidised form (the metabolite glycine betaine) contributes to S-adenosylmethionine synthesis – a chief

methyl donor involved in DNA and histone methylation which play a central role in regulating gene expression and potentially modulating brain function.<sup>9,10</sup> Choline also influences liver function, with shortfalls linked to defective lipoprotein metabolism, abnormal phospholipid synthesis and oxidative damage.<sup>11</sup>

Low oestrogen status (oestrogen catalyses phosphatidylcholine conversion to choline via the phosphatidylethanolamine-N-methyltransferase; PEMT enzyme) and genotype (eg, polymorphisms in the PEMT gene) can both alter choline dietary requirements.<sup>12</sup> For the latter, a growing body of evidence exists suggesting that choline requirements may depend on the presence of several genotypes and that individuals with these could well have choline requirements higher than current recommended intakes.<sup>13,14</sup>

The risk of choline inadequacies, either due to low habitual intake or gene polymorphisms, is particularly concerning at key stages of the life cycle such as pregnancy and lactation. Choline is actively transported to the fetus in utero, with maternal supplies correlating with cognitive outcomes.<sup>15</sup> This nutrient is particularly critical during fetal development as it modifies brain and spinal cord structure (via apoptosis and stem cell proliferation) influencing the risk of lifelong memory function and possible risk of neural tube defects.<sup>16</sup>

In pregnancy, choline supplementation at about twice the recommended amount (930 mg) improves infant information processing speed.<sup>17</sup> It has also been suggested that additional choline could improve affective, cognitive and neural functioning when taken by mothers carrying a fetus with Down syndrome.<sup>18</sup> Among lactating mothers, both intake of choline and genetic polymorphisms influence choline concentrations in human breast milk, subsequently impacting on levels transferred to the infant.<sup>19</sup> Human neonates are also born with choline blood levels around



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**Table 1** United States Institute of Medicine and European Food Safety Authority Adequate Intake recommendations for choline

Life stage	US IOM (1998) AI (mg/day) <sup>1</sup>			EFSA (2016) AI (mg/day) <sup>2</sup>	
	Age (years)	Males	Females	UL (mg/day)	Age (years) AI
Adult	≥19	550	425	3500	≥18 years 400
Pregnancy	–	–	450	3500	480
Lactation	–	–	550	3500	520

AI, Adequate Intake; EFSA, European Food Safety Authority; IOM, Institute of Medicine; UL, Tolerable Upper Intake Level; US, United States.

three times higher than maternal levels, indicating high demands during this life stage.<sup>20</sup>

### Authoritative choline recommendations

Nearly two decades ago in 1998 it was the US IOM that first established choline intake recommendations.<sup>1</sup> As shown in table 1, the Adequate Intake (AI) for choline was set at 550 mg/day for males and 425 mg/day for non-pregnant females aged 19 years and over. This was based on amounts that prevented hepatic dysfunction in human studies, defined as elevated aminotransferase in serum. For pregnancy and lactation, increments were added for fetal and placental accumulation and choline output in mature milk, increasing requirements to 450 and 550 mg/day, respectively.

More recently in 2016 the EFSA<sup>2</sup> re-evaluated the evidence and also compiled dietary requirements for choline. Once again AIs were compiled, with these being set at 400 mg/day for all adults, based on observed average choline intakes in healthy European populations and after considering the amount of choline needed to replete around 70% of depleted subjects in a depletion/repletion study. Again, upward adjustments were made for pregnant and breastfeeding women to account for the mean gestational rise in body weight and lactation based on the amount of choline in human milk during the first 6 months of exclusive breastfeeding. Thus, intakes of 480 and 520 mg/day are advised for pregnancy and lactation, respectively.

In 2011 the EFSA<sup>21</sup> authorised a number of choline-related health claims. It was concluded that a cause and effect relationship had been established between the following: (1) “choline is needed for lipids metabolism”, (2) “maintaining healthy liver functioning” and (3) “reduction in homocysteine levels”. At that time evidence in relation to choline consumption and the maintenance of normal neurological function, cognitive function or brain and neurological development was not thought to be sufficient.

### Food sources and changing trends

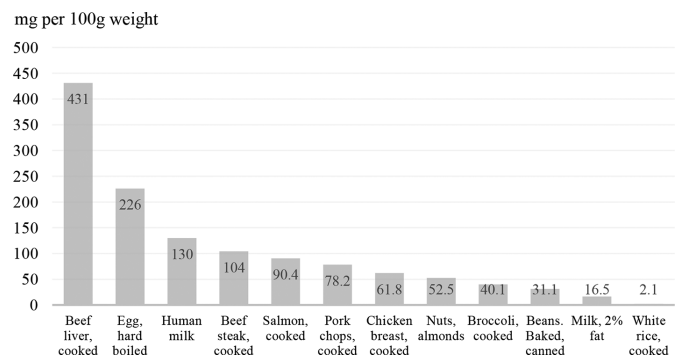
It is well appreciated that animal foods contain more choline per unit weight than plant sources.<sup>22</sup> In general, beef, eggs, fish, chicken, nuts, milk and certain plant foods such as cruciferous broccoli provide some dietary choline.<sup>23</sup> Other examples of food sources providing choline and the amount per 100 g are shown in figure 1.

Relevantly, European research<sup>24</sup> has shown that habitual choline intakes are, on average, below the AI established in 1998 by the IOM, and that meat, milk, eggs, grains and their derived products were the predominant sources of dietary choline.

In one publication<sup>25</sup> using US National Health and Nutrition Examination Survey data (NHANES; 2009–2014 datasets) achievement of the AI for choline was extremely difficult without the consumption of eggs or taking a dietary supplement. For example egg consumers had almost twice the usual choline intake compared with non-consumers. The survey also showed that protein, meat and seafood consumption were associated with increased choline intakes compared with non-consumers. In the UK such an analysis has not been conducted, although red meat and processed meat intakes among those aged 19–64 years have declined by 19 g over the last 9 years.<sup>26</sup>

Other work<sup>27</sup> based on the NHANES datasets showed that only around 11% of American adults achieve the IOM AI for choline. In Europe it has also been found that average choline intakes are below AI thresholds set by the IOM.<sup>23</sup> In Alberta, Canada one study<sup>28</sup> showed that only 23% of pregnant women and 10% of lactating mothers (n=600) met the choline AI recommendation and that the main dietary sources of choline were eggs, dairy products and meat. Women consuming at least one egg daily were eight times more likely to meet choline intake recommendations compared with pregnant non-consumers.

This is interesting yet equally concerning given that current trends appear to be towards meat reduction and plant-based diets.<sup>29 30</sup> The recent 2019 EAT-Lancet<sup>31</sup>



**Figure 1** Different food sources providing choline. Values are for total choline, the sum of individual choline forms. Source: data extracted from Wiedeman *et al* (2018).<sup>23</sup>

publication has compiled a healthy reference diet, based on an adult dietary intake of 2500 kcal/day. While this should be praised in that it is the first report to compile a healthy food plan based on promoting environmental sustainability, restricted intakes of whole milk, eggs and animal protein could impact on choline intakes and status. For example, just 7 g beef and lamb, 13 g egg and 250 g whole milk or derivative equivalents such as cheese are advised, although ranges are also provided. Given the acceleration of these dietary trends, their impact on choline intakes is a crucial area worthy of consideration and further study.

### The need for more research in the UK

Given the important physiological roles of choline and authorisation of certain health claims it is questionable why choline has been overlooked for so long in the UK. Choline is presently excluded from UK food composition databases, major dietary surveys and dietary guidelines. In Australia, for example, the AUSNUT 2011–13 database<sup>32</sup> has now been expanded to include Australian choline values. Composite foods, and ‘not further-specified foods’, were developed using the Food Standards Australia New Zealand (FSANZ) recipe files, and when applied it was discovered that less than 10% of the population were found to achieve the AI for choline (eggs again ranked top as a contributor).

Similar approaches could be adopted to the UK McCance and Widdowson database<sup>33</sup> as a starting point for quantifying habitual choline intakes in the UK. This database was recently updated in 2019 but choline was not included. These data could then be embedded, used to quantify habitual intakes in the UK, and be reported alongside other B vitamins such as folate in the National Diet and Nutrition Survey. Likewise, now the time may also be right for a Scientific Advisory Committee on Nutrition call, relating to the inclusion of choline as part of UK Dietary Guidelines.

### Summary and perspective

The mounting evidence of choline’s importance makes it essential that it does not continue to be overlooked in the UK. This is now more important than ever given that accelerated food trends towards plant-based diets/veganism could have further ramifications on choline intake/status. Government bodies and organisations should look to extended datasets to include this essential nutrient. So far, looking at the evidence-base we know that:

- ▶ Choline is a critical nutrient needed for neurocognition, lipid metabolism, liver function and homocysteine regulation.
- ▶ The majority of Europeans, American, Canadian and Australian populations are not meeting choline AI recommendations.
- ▶ Eggs, milk and meat appear to be major dietary providers and further movements away from the

consumption of these could have unintended consequences for choline intake/status.

- ▶ Ongoing nutrition research must study ‘long-term’ intakes of choline e.g. using food frequency questionnaires rather than 24-hour recalls, which will give a more reliable picture of choline intakes.
- ▶ More needs to be done to educate health care professionals and consumers about the importance of a choline-rich diet and how to achieve this.
- ▶ If choline is not obtained in the levels needed from dietary sources per se then supplementation strategies will be required, especially in relation to key stages of the life-cycle such as pregnancy, when choline intakes are critical to infant development.<sup>34</sup>

**Correction notice** This article has been corrected since it was published online. The ‘Competing interests’ section has been updated.

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### **Suggested move to plant-based diets risks worsening brain health nutrient deficiency**

*And UK failing to recommend or monitor dietary levels of choline, warns nutritionist*

The momentum behind a move to plant-based and vegan diets for the good of the planet is commendable, but risks worsening an already low intake of an essential nutrient involved in brain health, warns a nutritionist in the online journal **BMJ Nutrition, Prevention & Health**.

To make matters worse, the UK government has failed to recommend or monitor dietary levels of this nutrient--choline--found predominantly in animal foods, says Dr Emma Derbyshire, of Nutritional Insight, a consultancy specialising in nutrition and biomedical science.

Choline is an essential dietary nutrient, but the amount produced by the liver is not enough to meet the requirements of the human body.

Choline is critical to brain health, particularly during fetal development. It also influences liver function, with shortfalls linked to irregularities in blood fat metabolism as well as excess free radical cellular damage, writes Dr Derbyshire.

The primary sources of dietary choline are found in beef, eggs, dairy products, fish, and chicken, with much lower levels found in nuts, beans, and cruciferous vegetables, such as broccoli.

In 1998, recognising the importance of choline, the US Institute of Medicine recommended minimum daily intakes. These range from 425 mg/day for women to 550 mg/day for men, and 450 mg/day and 550 mg/day for pregnant and breastfeeding women, respectively, because of the critical role the nutrient has in fetal development.

In 2016, the European Food Safety Authority published similar daily requirements. Yet national dietary surveys in North America, Australia, and Europe show that habitual choline intake, on average, falls short of these recommendations.

“This is....concerning given that current trends appear to be towards meat reduction and plant-based diets,” says Dr Derbyshire.

She commends the first report (EAT-Lancet) to compile a healthy food plan based on promoting environmental sustainability, but suggests that the restricted intakes of whole milk, eggs and animal protein it recommends could affect choline intake.

And she is at a loss to understand why choline does not feature in UK dietary guidance or national population monitoring data.

“Given the important physiological roles of choline and authorisation of certain health claims, it is questionable why choline has been overlooked for so long in the UK,” she writes. “Choline is presently excluded from UK food composition databases, major dietary surveys, and dietary guidelines,” she adds.

It may be time for the UK government's independent Scientific Advisory Committee on Nutrition to reverse this, she suggests, particularly given the mounting evidence on the importance of choline to human health and growing concerns about the sustainability of the planet's food production.

"More needs to be done to educate healthcare professionals and consumers about the importance of a choline-rich diet, and how to achieve this," she writes.

"If choline is not obtained in the levels needed from dietary sources per se then supplementation strategies will be required, especially in relation to key stages of the life cycle, such as pregnancy, when choline intakes are critical to infant development," she concludes.