NICE National Institute for Health and Care Excellence

Expert testimony to inform NICE guideline development

Section A: Developer to complete	
Name:	Dr Maggie Blott
Role:	Obstetrician
Institution/Organisation (where applicable): **Contact information:**	Royal Free London NHS Foundation Trust
Guideline title:	Vitamin B12 deficiency in over 16s: diagnosis and management
Guideline Committee:	Vitamin B12 deficiency
Subject of expert testimony:	Diagnosis and management of vitamin B12 deficiency during pregnancy and breastfeeding
Evidence gaps or uncertainties:	How do diagnosis and management differ during pregnancy and breastfeeding compared to the general population? Below is more detail on questions the committee asked

Supplementary information supplied with initial request on 12th April 2023

A summary of the draft recommendations on 12th April 2023:

- Use total or active B12 test if vitamin B12 deficiency is suspected. Interpret results with caution in pregnant and breastfeeding women as changes in the body will alter B12 levels which don't necessarily mean there is a deficiency.
- Treatment – follow 'standard population' recommendations for newly diagnosed pregnant and breastfeeding women. Continue current treatment for those already receiving treatment for a B12 deficiency.

A summary of the 'standard population' recommendations are:

- Dietary vitamin B12 deficiency – dietary advice for everyone
- Dietary vitamin B12 deficiency and moderate or severe symptoms:
    - consider oral B12 replacement, or
    - consider intramuscular injections (off-label) if there are concerns about adherence (e.g. dementia)
- Dietary advice – if oral isn't working consider intramuscular injections (off-label)
- Medicine induced deficiency – intramuscular injections (off-label) while taking the medicine or change the medicine if that is possible
- Vitamin B12 deficiency due to malabsorption:
    - Offer intramuscular injections if they have or are strongly suspected of pernicious anaemia, major gastric resection, bypass or terminal ileal

resection (offer as this is current practice and cheaper than oral)

- Consider intramuscular injections if they have vitamin B12 deficiency because of malabsorption that is not caused by pernicious anaemia or gastric surgery (consider because evidence is not clear)

Section B: Expert to complete

Summary testimony: [Please use the space below to summarise your testimony in 250–1000 words. Continue over page if necessary]

This statement includes response to the initial email request plus responses to subsequent queries.

Women already receiving vitamin B12 replacement

1. If the woman is already undergoing treatment for B12, she should continue through pregnancy and breastfeeding.
2. If there was a plan to stop B12 previously, perhaps because the cause was thought to be short term diet etc, continue the B12 until after breastfeeding then review the decision to stop the B12.
3. No obvious need to change an established dose in pregnancy.

When to suspect

4. Suspect vitamin B12 deficiency if:
    - the woman is high risk (vegetarian, inflammatory disease, prolonged use of pump inhibitors)
    - women with unexplained anaemia / poor response to iron
    - the woman has symptoms suggestive of B12 deficiency

These are the common causes and the list is not completely exhaustive.

Diagnosis

5. If clinical B12 deficiency is suspected in pregnancy:
    - Measure active B12 (Holotranscobalamin HTC) as a marker for B12 deficiency rather than total B12
    - Suggested cut off level in pregnancy < 35pmol/L
    - There is no guidance on indeterminate test results. If in doubt I would discuss with a haematologist to decide whether to commence treatment.
6. Perform Anti-intrinsic factor anti body test (IF-Ab)
    - If IF-Ab positive, commit to lifelong B12 and ask a gastroenterologist
    - If IF-Ab negative, stop B12 replacement after breastfeeding and then monitor B12 levels/MMA and probably ask whoever was the local B12 expert for a correct diagnosis
7. **Specific query from the committee:** Related to testing they wanted to know what your thoughts are on using methylmalonic acid (MMA) for testing in pregnancy? The biochemists on the committee noted MMA concentrations may go up during pregnancy and therefore may not be as reliable as active B12. Is this your understanding too?
   Response: MMA levels do go up in pregnancy but they also go up in B12 deficiency. I think you will need to ask a haematologist.

Treatment

8. If diet related B12 deficiency, oral cyanocobalamin (suggested oral doses 1000 mcg daily). Repeat test after 4 weeks to ensure a response.
9. IM route if B12 deficiency is not diet related or very severe. Start with a loading dose followed by a replacement regimen through the rest of pregnancy and breastfeeding, every 8-12 weeks, or combination of the two. No evidence of

superiority either way.

10. Consider recommending routine oral supplements at a lower dose (150mcg) for people who are vegetarian/vegan in pregnancy and breastfeeding

Nitrous oxide use during labour

11. If already on a B12 replacement regimen, either pre-existing the pregnancy or started in pregnancy, nitrous oxide during labour is very unlikely to be an issue and can be used on obstetric grounds.
12. If newly diagnosed with no time to start treatment at the time of labour (which is of course incredibly rare), probably nitrous oxide should be avoided. But even if vitamin B12 deficiency is diagnosed or suspected very late in pregnancy there would almost certainly be time to get sufficient B12 on board before labour.
13. **Specific query from the committee**: would someone on vitamin B12 replacement need an extra dose [extra to their normal regimen] either before or after nitrous oxide use during labour? **Response**: I have never come across this but it would only be relevant if newly diagnosed which in pregnancy is very unlikely.
14. **Specific query from the committee**: Does nitrous oxide use affect homocysteine concentrations? **Response**: I do not know the answer to this.

Other comments

15. If anything, the group at theoretically greatest risk are those with marginal B12 status who have never been diagnosed or replaced as asymptomatic, but we have no evidence of them coming to harm and routine testing is not advocated.
16. **Specific query from the committee:** Are you aware of what guidance obstetricians use when considering vitamin B12 deficiency in pregnant and breastfeeding women? Is it the BSH guidance? Also, if asked by other healthcare professionals are obstetricians likely to recommend these guidelines? We would do a sense check of our recommendations against these. **Response**: We do use these guidelines but in truth there is no specific guidance for management of B12 deficiency in pregnancy.

References to other work or publications to support your testimony' (if applicable):

Disclosure:
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Expert testimony papers are posted on the NICE website with other sources of evidence when the draft guideline is published. Any content that is academic in confidence should be highlighted and will be removed before publication if the status remains at this point in time.