Case Report ISSN 2768-6647

Medical and Clinical Case Reports

Vitamin B12, Nitrous Oxide Use During Labor and Autism

Gregory John Russell-Jones*

B12 Oils, Pty Ltd, Greenfield Ave, Middle Cove, Sydney, New South Wales, Australia.

***Correspondence:**
Dr. Russell-Jones G, B12 Oils, Pty Ltd, Greenfield Ave, Middle Cove, Sydney, New South Wales, Australia.

Received: 02 Jan 2026; **Accepted:** 11 Feb 2026; **Published:** 23 Feb 2026

Citation: Gregory John Russell-Jones. Vitamin B12, Nitrous Oxide Use During Labor and Autism. Med Clin Case Rep. 2026; 6(1): 1-7.

ABSTRACT

Introduction: *Metabolic analysis has been performed on 5 children who have been diagnosed with autism (developmental delay), and who were born to mothers who used nitrous oxide for pain relief during labour. The analysis showed elevated levels of the methylB12 deficiency markers, HVA, VMA, QA and pyroglutamic acid, supporting the notion that there had been extensive inactivation of the enzyme methionine synthase. The results are consistent with the known ability of nitrous oxide to form NO-Co(III)cobalamin, which subsequently irreversibly inactivates the enzyme methionine synthase. The data contradicts the contention of many obstetricians and maternity staff that Nitrous oxide is harmless to the mother and baby. The findings are consistent with the hypothesis that it is the increased usage of nitrous oxide during labor that is responsible for the 30-fold increase in the rate of autism in the past 30 years. The findings strongly suggest that nitrous oxide should be banned during labor.*

Summary: *Studies of children with autism who were born to mothers who used nitrous oxide for pain relief during delivery, have shown that the nitrous oxide has inactivated the vitamin B12, and subsequently the presence of inactive vitamin B12 has led to the developmental delay.*

Keywords
Autism, Vitamin B12, Nitrous oxide, Labor.

Introduction
Over the past 40 years there has been a dramatic increase in the rate of autism, and in many countries the rate has increased from around 0.1% to current rates of 3% and above. During this time, there has also been a huge increase in the rate of use of nitrous oxide in mothers during labor. Formerly only around 1% of babies were born to mothers who were administered nitrous oxide as a pain medication during labor, whereas more recently this rate has increased to over 50% in countries such as the UK, USA and Australia. The administration of nitrous oxide has for some reason, totally ignored the known association between nitrous oxide use, and inactivation of vitamin B12, particularly Co(I)cobalamin. Methylation in the body is dependent upon the methylation cycle in which S-Adenosylmethionine donates the methyl group on methionine to a methyl receiver such as a neurotransmitter, a peptide, DNA, or other molecular receiver. In the reaction S-adenosylmethionine (SAM) is converted to S-adenosylhomocysteine (SAH), and then homocysteine. Regeneration of methionine, as part of the methyl cycle, requires the action of the action of the enzyme, methionine synthase which uses MethylCo(III)cobalamin as a cofactor to donate the methyl group to homocysteine, thereby regenerating methionine.

MethylCo(III)B12 [Methionine Synthase] + Homocysteine <=> **Co(I)B12** [Methionine Synthase] + Methionine
In order to continue the cycle MethylCo(III)B12 must be regenerated, which occurs through the donation of the methyl group from 5-methyltetrahydrofolate (5MTHF) to Co(I)B12.

Co(I)B12[Methionine Synthase] + 5MTHF <=> **MethylCo(III)B12**[Methionine Synthase] + THF A limited amount of 5MTHF can be obtained from diet, but the major source of 5MTHF comes from within the folate cycle.

Serine + THF [Serinehydoxymethyl Transferase][P5P] ⇔ Glycine + 5,10-methylene-THF.

Notable in the reaction is the requirement for active vitamin B6 (P5P) for the activity of SHMT. 5,10-methylene-THF is then reduced to 5-methyl-THF by the B2/B3 dependent enzyme methionine-tetrahydrofolate reductase (MTHFR)
5,10-methylene-THF [MTHFR][FAD/NADPH] ⇔ 5-methyl-THF

Hence the ability to regenerate methylCo(III)B12 is critically dependent upon 5MTHF, and more importantly active vitamin B2/B3 and vitamin B6. In the absence of incoming 5MTHF, **Co(I)B12** is rapidly oxidized to inactive **Co(II)B12**. Lack of 5MTHF would occur in deficiency of folate, or functional B2 (FMN and FAD) and/or B3. **MethylCo(III)B12** can be regenerated from **MethylCo(III)B12** through the action of the B2/B3 dependent enzyme Methionine Synthase Reductase (MTRR).

Co(II)B12 + SAM [Methionine Synthase Reductase][FMN/FAD/NADH] <=> **MethylCo(III)B12** + SAH
Thus, it can be seen that the methylation cycle is critically dependent upon vitamin B6, B2, B3 and Cobalamin. The reactions of MTHFR and MTRR are significantly reduced in the absence of active B2, and in addition mutations in the two enzymes, MTHFR and MTRR and in particular the two common mutations, MTHFR A66G and MTRR C667T.

Additional problems occur during birthing, particularly if the mother uses Nitrous Oxide as a sedative. Nitrous Oxide attacks **Co(I)B12** to irreversibly form the biologically inactive **NO-Co(III)B12**. The enzyme-bound NO-Co(III)B12 totally inactivates the enzyme Methionine Synthase, thereby leading to Methyl B12 deficiency. It has been known for over 40 years that vitamin B12 deficiency in the neonate is responsible for developmental delay and failure to thrive. Poisoning with Nitrous is rather insidious as the serum levels of vitamin B12 are normal or elevated and as such functional B12 deficiency is missed.

As early as 1978 [1-6] the use of nitrous oxide for anaesthesia was found to be contra-indicated, yet to this day it is still used, and many individuals report signs of B12 deficiency following use. Unbelievably, despite numerous publications showing poor outcomes of nitrous oxide use in pregnancy, and several demonstrating an association between nitrous and autism, and over 100 publications, demonstrating inactivation of vitamin B12 by nitrous oxide, with subsequent sequelae, clinicians in the US, UK and Australia claim “Initiation and management of nitrous oxide by registered nurses is a safe and cost-effective option for labour pain”. This though is not the case. The use of nitrous oxide in pregnancy has shown a dramatic increase over the past 30 years, with an increase from less than 1% of births to now as many as 50% births, with the mothers being informed that nitrous oxide is perfectly safe. During that time the incidence of autism has risen from less than 0.1% of births, to a current rate of 3% (USA, UK, Australia). In this study, we report the drastic outcome for five children, who have the MTRR+/+ mutation, who were born to mothers who were not informed of the risk of nitrous oxide during delivery, and delivered what appeared to be healthy children who subsequently were diagnosed with autism. Years later, these children (8, 8, 10, 10 and 17 years old) still have developmental delay, and despite daily treatment with vitamin B12 for four years, have not been able reduce their markers of methyl B12 deficiency.

Methods

Study sample data analysis was carried out under the Australian National Health and Medical Research Council guidelines (NHMRC). Under these guidelines, all data was de-identified and steps were taken to ensure the anonymity and confidentiality of the data. De-identification has consisted of absolute anonymity and confidentiality of the data, such that no specifics such as gender, ethnicity, Country of Origin, etc., is associated with any data point in the study.

As such per the NHMRC guidelines: 1. The research does not carry any risk to the participants 2. The benefits of the research are many and will be of considerable benefit to any past, current or future participants, and as such represent no harm. 3. The participants had been notified at the time of analysis that data presented for analysis might potentially be used in research – but would be totally de-identified (which it has been). 4. Given the total de-identification of the data, there is absolute protection of their privacy 5. Data is only housed in one location and has only been assessed by one person, and as such the confidentiality of the data can be assured. 6. No financial benefits from the data are anticipated, rather the data will be used to help prevent and treat those to whom the data applies. 7. The waiver is not prohibited by State, Federal or International Law. A retrospective analysis was performed upon data submitted to us for analysis from children who had been diagnosed with ASD from countries including USA, United Kingdom, Canada and Australia. No selection was made in the acceptance of data, with no data being rejected. We were not made privy to either the methods of assessment nor of the severity of the Developmental Delay in the Children. Data is presented regardless of sex, or age. Metabolic analysis was performed on Organic Acid Test Data (Great Plains Laboratories, Lenexa, KS, USA), which had been submitted to us for interpretation, by parents of children with autism spectrum disorder. Data from the 5 children with autism was compared to a person who was healthy, and who had no previously identified health condition (NT). Data was tabulated in an Excel spreadsheet, and processed using the standard plotting functions in the program. Individual data is plotted as Scattergrams (Figures 1-3). Correlations for the 3 nitrous oxide children are plotted separately.

Urinary Organic Acids Testing (Oasis diagnostics) was used to compare the Adenosyl B12 (Adenosylcobalamin) deficiency marker, MMA (methylmalonic acid), with 4 methyl B12 deficiency markers HVA (homovanillic acid, VMA (vanillylmalonic acid), QA (quinolinic acid) and pyroglutamic acid.

Results

Initial diagnosis ascertained that all children had functional B12

deficiency by many markers in OAT, including MMA, HVA, VMA, QA, and pyroglutamic acid.

Comparison of MMA levels (a marker of Adenosyl B12 deficiency), with HVA (a marker of Methyl B12 deficiency (Figure 1) between 5 nitrous affected children showed little correlation between HVA and MMA, whereas there was a linear correlation between HVA and MMA in the neurotypical subject.

When the two sets of data were compared, it was noted that there was a higher range of MMA values in the autism group (Figure 2 left panels), as well as the lack of correlation between the methyl B12 deficiency markers and MMA in the autism group. In contrast there were lower MMA values and better correlations in the neurotypical data (Figure 2 Right panels). The data suggests that nitrous oxide is affecting methyl B12 levels more than adenosyl B12 levels.

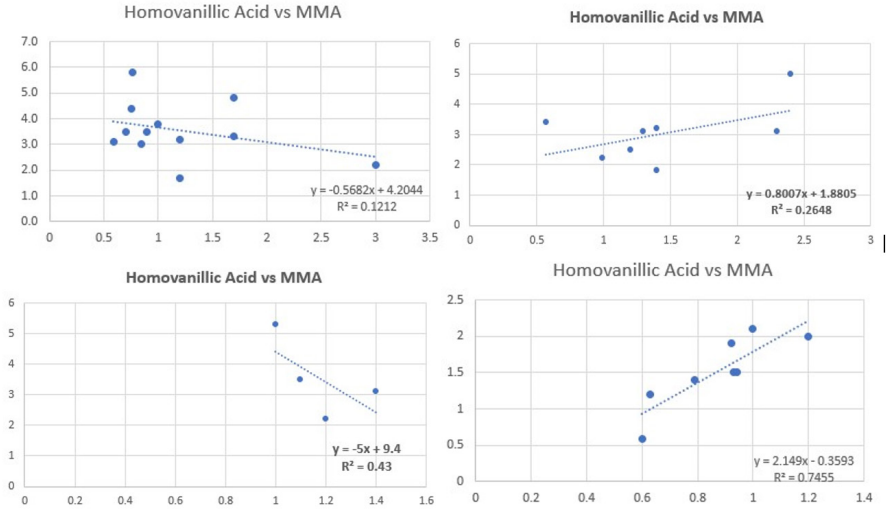

Figure 1: Comparison of several data points from three nitrous affected children (top left, top right, and bottom left), with a neurotypical subject (bottom right).

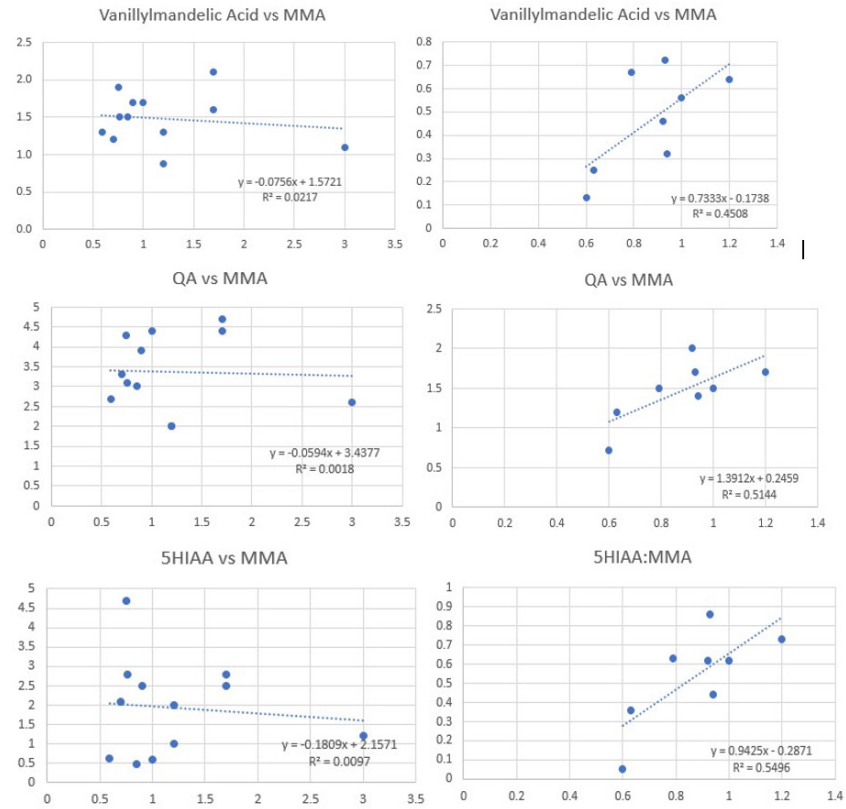

Figure 2: Comparison of multiple measurements of neurotransmitter metabolites associated with methyl B12 deficiency (HVA, QA, 5HIAA), with MMA, a marker of Adenosyl B12 deficiency. Left panels, multiple data points from an autistic child of a mother who used nitrous. Right panels multiple data points from a neurotypical individual.

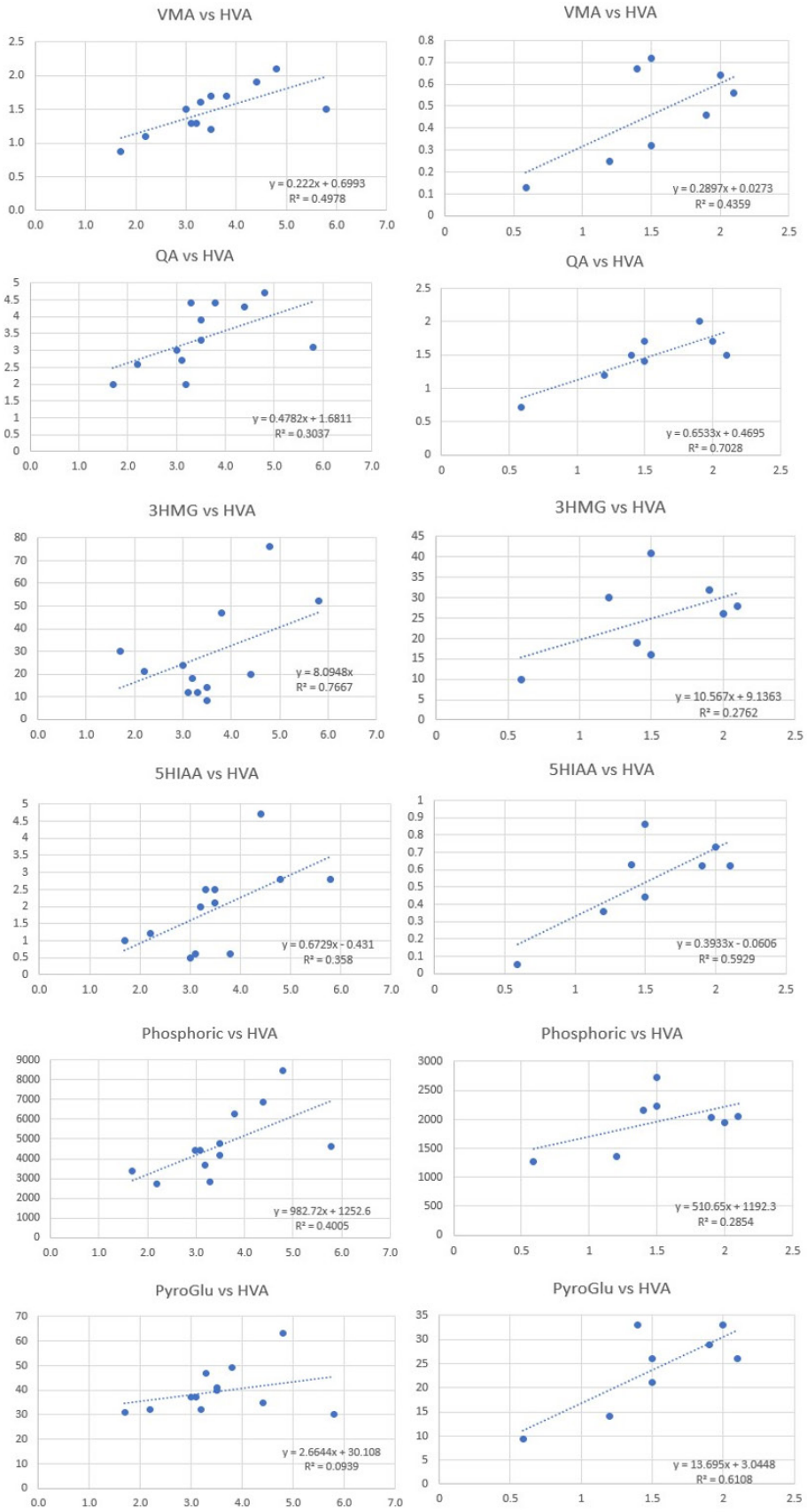

Figure 3: Comparison of HVA and VMA, QA, 3HMG, 5HIAA, and phosphoric acid correlations in the ASD subject (Left Panels) and the neurotypical data (Right panels).

In contrast to the data comparing MMA to methyl deficiency markers, it was found that both the ASD and the neurotypical subject, there were good correlations between HVA and VMA, QA, 3HMG (3-hydroxymethylglutamic acid), 5HIAA (5-hydroxyindole acetic acid), and phosphoric acid (Figure 3). The exception was pyroglutamate and HVA, where there appeared to be lack of active sulphation pathway in the ASD individual as judged by higher, unresolved pyroglutamate levels.

Comparison of the levels of MMA and HVA showed a distinct difference between the nitrous exposed children, where the ratio was between 7:1 to 0.8:1.0, In contrast in the neurotypical subject the ratio was 1:1 initially, peaking at 2:1, and staying below 2:1 (Figure 4). Further, the levels of HVA were generally above 3 mmol/L, in contrast levels of HVA were trending to 1 mmol/L in the neurotypical subject.

Data from all five children was pooled and analysed for relationship between the adenosyl B12 deficiency marker MMA, and them B12 deficiency markers, HVA, VMA, QA and pyroglutamic acid (See Figure 5, below).

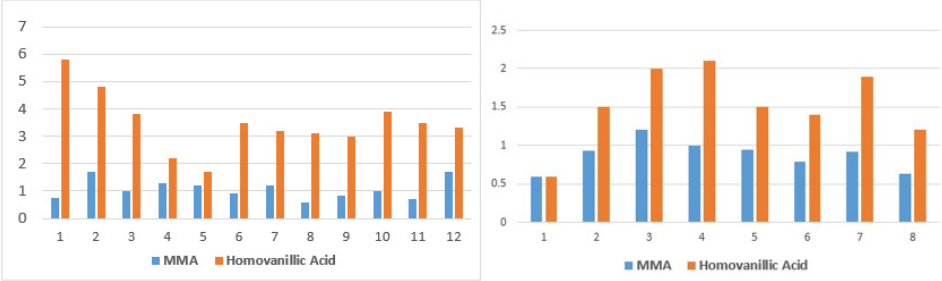

Figure 4: Comparison of MMA: HVA levels in sequential measurements from a Nitrous exposed child (left panel), to the neurotypical subject (right panel).

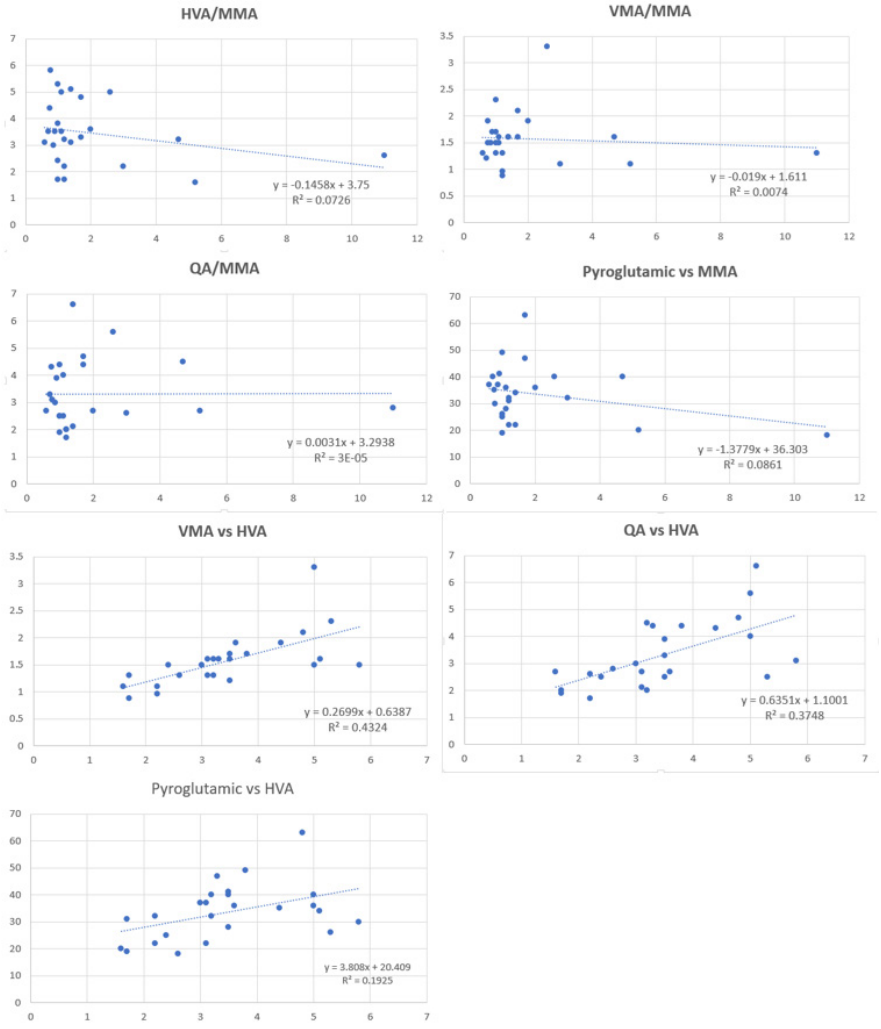

Figure 5: Comparison of MMA to HVA, VMA, QA and pyroglutamate, and HVA to VMA, QA, and pyroglutamate.

Pooled data from five nitrous exposed children showed little correlation between the standard adenosyl B12 deficiency marker (MMA), and four of the standard methyl B12 markers (HVA, VMA, QA and pyroglutamate) (Figure 5). In contrast, there was a correlation within the methyl B12 deficiency markers VMA, QA and pyroglutamate and HVA. The data would support the hypothesis that nitrous oxide preferentially reduces the activity of methionine synthase.

Discussion

The effect of nitrous oxide (N2O) on vitamin B12 is greater in those who have low vitamin B12 at birth [7], or in those that have functional vitamin B2 deficiency, which leads to functional B12 deficiency. Studies have shown that vitamin B12 insufficiency during pregnancy is common even in non-vegetarian populations and that concentrations of vitamin B12 decrease from the first to the third trimester [8] Studies in individuals who have had nitrous intoxication due to the use of "Nangs" have shown that the resultant sequelae can be very long lasting, with many individuals not recovering from the intoxication [9-13]. In many individuals serum B12 and holotranscobalamin are normal or elevated but there is an increase in MMA and homocysteine [14], a condition of paradoxical B12 deficiency [15]. Hence, progression of N2O-induced peripheral neuropathy with damage to the spinal cord can result in irreversible damage in an adult. One would expect much more severe pathology in a neonate. It is known that the effect of N2O is worse in those who are B12 or functionally B12 deficient. Studies have also shown that the effect of nitrous is worse in those with deficiencies in MTHFR and MTRR genetic variants [16]. Of note, human fetal/neonatal and geriatric kinetics of inactivation and reactivation are unknown in any tissue. N2O inhibition of methionine synthase is rapid, potent, and irreversible in all patients, and harmful in a substantial proportion of patients that are not identified before exposure. Inaction would become progressively worse with an increase in time and dose of exposure.

The data presented supports the findings of other workers, who have contended that "There is a growing body of evidence that supports avoidance of nitrous oxide in both paediatric and adult patients", [17,18]. These concerns have led some departments to cease the use of Nitrous oxide all together [19]. It has been known for 30 years that, nitrous oxide given as pain relief during labour was shown to inhibit methionine synthase in the placenta in a dose- responsive manner [7]. Further, use of nitrous oxide in children has also been shown to raise homocysteine levels in the children, indicative of inactivation of vitamin B12 [20]. Studies in guinea pigs have shown the anaesthetics such as fluorophaned plus nitrous oxide can cause permanent damage to the fetal brain [21]. Early studies have shown rapid transfer of nitrous oxide across the placenta into the umbilical vein, with levels reaching 90% of maternal serum levels [22]. In the current study, metabolic analysis of 5 children, born to mothers who used nitrous oxide for pain relief during labour, and who were diagnosed with developmental delay showed various degrees of methyl B12 deficiency, which lasted for many years following birth. The data is consistent with that of Ljungblad and co-workers [23], who found elevated MMA and homocysteine in blood samples from children born to mothers who used nitrous, and was predictive of the children later developing vitamin B12 deficiency. The data is also consistent with the observations of Russell-Jones [15] who has found that every child with autism assayed by his group was functionally deficient in vitamin B12. This deficiency was paradoxical in that serum B12 was normal or elevated [24]. The increased rate of autism, from 0.1% to 3% from 1980 to 2025 in the US and Australia, is consistent with the increased use of nitrous oxide in mothers during labour from 1% to 50% or more. Given the ever increasing rate of autism, with the ever increasing costs associated with what has been deemed a life-time of condition, it would seem logical and indeed prudent to BAN the use of Nitrous oxide during labour.

Summary

Metabolic analysis of 5 children, born to mothers who used nitrous oxide during labour, and who were subsequently diagnosed with developmental delay, revealed elevated markers of both adenosyl and methyl B12 deficiency. Methyl B12 deficiency markers, were however, disproportionally high, supporting the concept that nitrous oxide reacts with Co(I)B12 to form biologically inactive NOCo(III)B12, with resultant inactivation of methionine synthase. All mothers had been told at time of labour that nitrous was safe and would not harm their children. The data presented strongly refutes the claims that the use of nitrous oxide during labour is harmless. The data strongly supports the notion that the use of nitrous oxide during labour should be totally avoided, with the practise banned forthwith.

References

1. Amess JA, Burman JF, Mollin DL. Nitrous oxide and bone-marrow. Lancet. 1978; 2: 740.
2. Cullen MH, Rees GM, Nancekievill DG, et al. The effect of nitrous oxide on the cell cycle in human bone marrow. Br J Haematol. 1979; 42: 527-534.
3. Amos RJ, Amess JA, Hinds CJ, et al. Incidence and pathogenesis of acute megaloblastic bone-marrow change in patients receiving intensive care. Lancet. 1982; 2: 835-838.
4. Amos RJ, Amess JA, Nancekievill DG, et al. Prevention of nitrous oxide-induced megaloblastic changes in bone marrow using folinic acid. Br J Anaesth. 1984; 56: 103-107.
5. Amos RJ, Amess JA, Hinds CJ, et al. Investigations into the effect of nitrous oxide anaesthesia on folate metabolism in patients receiving intensive care. Chemioterapia. 1985; 4: 393-399.
6. Sourial NA, Amess JA, Amos RJ. Role of S-adenosylmethionine in DNA synthesis and haemopoiesis. Scand J Haematol. 1985; 34: 303-307.
7. Landon MJ, Creagh- Barry P, McArthur S, et al. Influence of vitamin B12 status on the inactivation of methionine synthase by nitrous oxide. Br J Anaesth. 1992; 69: 81- 86.
8. Sukumar N, Rafnsson SB, Kandala NB, et al. Prevalence of vitamin B-12 insufficiency during pregnancy and its effect on

offspring birth weight: a systematic review and meta-analysis. Am J Clin Nutr. 2016; 103: 1232-1251.

9. Brunt TM, van den Brink W, van Amsterdam J. Rare but relevant: Nitrous oxide and peripheral neurotoxicity, what do we know? Addiction. 2025; 120: 1046-1050.
10. Boulin F, Bédat-Millet AL, Didier-Laurent A, et al. Neurological damage from recreational nitrous oxide use: Two distinct electroclinical profiles in a retrospective cohort. Rev Neurol (Paris). 2025; 181: 742-747.
11. Einsiedler M, Voulleminot P, Demuth S, et al. A rise in cases of nitrous oxide abuse: neurological complications and biological findings. J Neurol. 2022; 269: 577-582.
12. Zheng D, Ba F, Guorong B et al. The sharp rise of neurological disorders associated with recreational nitrous oxide use in China: A single-center experience and a brief review of Chinese literature. J Neurol. 2020; 267: 422-429.
13. Xiang Y, Li L, Ma X, et al. Recreational nitrous oxide abuse: Prevalence, neurotoxicity, and treatment. Neurotox Res. 2021; 39: 975-985.
14. Meißner JN, Neuneier J, Bartzokis I, et al. Increase of nitrous oxide-induced neurological disorders – a German multicenter experience. Neurol Res Pract. 2025; 7: 3.
15. Russell-Jones G. Paradoxical Vitamin B12 Deficiency: Normal to Elevated Serum B12, With Metabolic Vitamin B12 Deficiency. J Biol Today's World. 2022; 11: 001-004.
16. Selzer RR, Rosenblatt DS, Laxova R, et al. Adverse Effect of Nitrous Oxide in a Child with 5, 10-Methylenetetrahydrofolate Reductase Deficiency. N Engl J Med. 2003; 349: 45-50.
17. Schmitt EL, Baum VC. Nitrous oxide in pediatric anesthesia: friend or foe? Curr Opin Anaesthesiol. 2008; 21: 356-359.
18. Baum VC. When nitrous oxide is no laughing matter: nitrous oxide and pediatric anesthesia. Paediatr Anaesth. 2007; 17: 824-830.
19. Schwilden H, Schüttler J. 200 years of nitrous oxide (laughing gas)--and the end of an era? Anasthesiol Intensivmed Notfallmed Schmerzther. 2001; 36: 640.
20. Pichardo D, Luginbuehl IA, Shakur Y, et al. Effect of nitrous oxide exposure during surgery on the homocysteine concentrations of children. Anesthesiology. 2012; 117: 15-21.
21. Rizzi S, Carter LB, Ori C, et al. Clinical anesthesia causes permanent damage to the fetal guinea pig brain. Brain Pathol. 2008; 18: 198-210.
22. Mar X, Gertie FMD, Joshi CW, Orkin R. Placental Transmission of Nitrous Oxide. Anesthesiology. 1970; 32: 429-432.
23. Ljungblad UW, Lindberg M, Eklund EA, et al. Nitrous oxide in labour predicted newborn screening total homocysteine and is a potential risk factor for infant vitamin B12 deficiency. Acta Paediatr. 2022; 111: 2315-2321.
24. Russell-Jones G. Functional Vitamin B12 Deficiency in Autism. J Psychia. 2022; 25: 495.