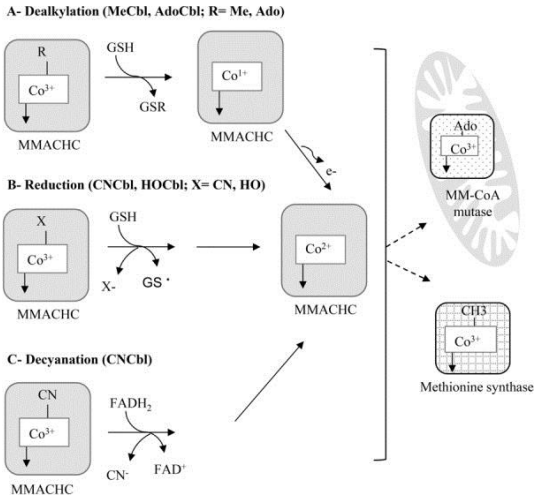
The Magic Methyl Myth

Why Methylcobalamin is no better than other forms of B12 and may be worse

Production of cob(II)alamin

Many places on the internet will tell you that there is something special about methylcobalamin supplements – that they are superior to other forms of B12, or that methylcobalamin specifically targets the nervous system. They are wrong.

In fact, all forms of B12, once they enter the cell, are equivalent. As soon as the B12 enters the cytosol it attaches to methylmalonic aciduria and homocystinuria type C protein (MMACHC) which catalyses the removal of the top ligand (methyl, cyano, hydroxo or adenosyl) to form cob(II)alamin.



From: [Cobalamin coenzyme forms are not likely to be superior to cyano- and hydroxyl-cobalamin in prevention or treatment of cobalamin deficiency]

From this point onwards, the cell cannot tell if you have been taking methylcobalamin or any other form of B12. They all form cob(II)alamin, which is then transported to the areas of the cell where it is required. Some goes to the mitochondria where it is converted to adenosylcobalamin. Some gets transported to the cytosol where it takes part in the conversion of homocysteine (hCys) to methionine (met).

Methionine synthase and methylcobalamin

The conversion of hCys to met is carried out by the enzyme methionine synthase. The first step in the process is the reduction of the cob(II)alamin produced from B12 to cob(I)alamin which binds to the methionine synthase enzyme. Then a molecule of methyltetrahydrofolate (MTHF) also binds to the enzyme. The methyl group of MTHF passes to the cob(I)alamin, producing enzyme-bound methylcobalamin and releasing tetrahydrofolate (THF). This binding activates the enzyme, allowing a molecule of hCys to bind to a zinc atom in the enzyme. The methyl group is passed from the methylcobalamin to the sulfur atom of the hCys to produce met, which is then released.

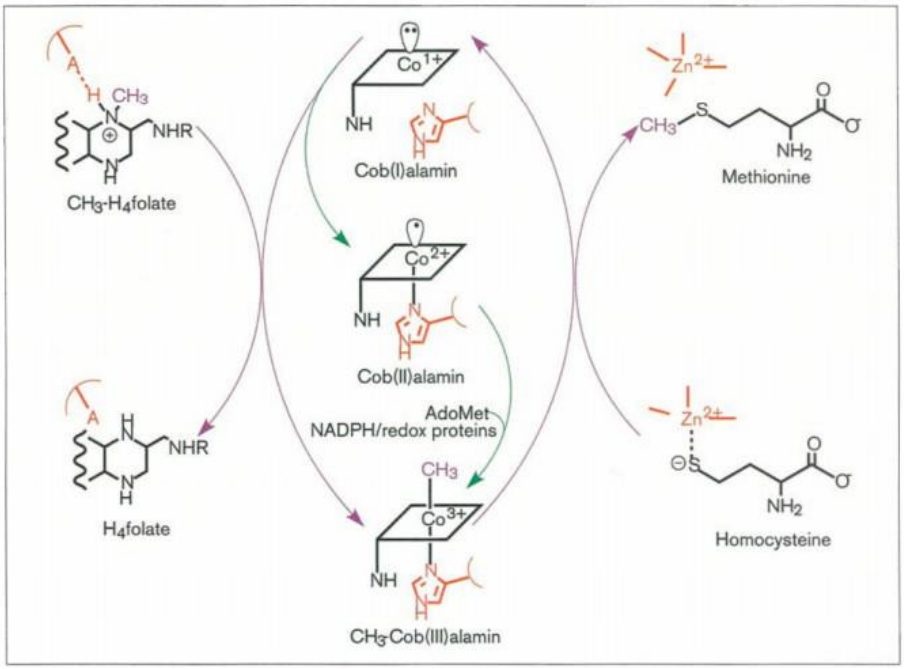


Image source: Cobalamin Biochemistry

From this it should be plain that methylcobalamin is unlikely to have any advantage over other forms of B12 in the treatment of a B12 deficiency. **Even if methylcobalamin could get into the cytosol intact, it would be incapable of binding to methionine synthase**.

Note: In about one in every 2000 cycles of the above reaction, the cob(I)alamin is not regenerated. Instead cob(II)alamin is formed. This inactivates the enzyme. The cob(I)alamin is regenerated by the enzyme MTRR. In the diagram above this is shown by the central pathway.

MTHFR and methylcobalamin

You will often find it said that people with certain mutations in a gene called MTHFR need to take methylcobalamin. This is demonstrably incorrect.

In the section above we saw how MTHF is required to donate a methyl group to cob(I)alamin. MTHF is formed by the reduction (addition of hydrogen) of methylenetetrahydrofolate (MeTHF). The enzyme responsible for this is called methylenetetrahydrofolate reductase, or MTHFR. The gene that codes for this enzyme is also called MTHFR.

This gene, like all other genes, is subject to mutations. Indeed, it is likely that you have at least one mutation on this gene. However, like most other mutations, they tend not to have any effects at all. Indeed, the only mutation shown, by repeatable, reputable, scientific studies, to have any possibility of an adverse effect is homozygous (two copies) of the C677T mutation. That's according to one of the largest genetic testing companies in the world.

This mutation, which is carried by about 9% of the population, doesn't stop the production of MTHF. It does make the MTHFR enzyme less stable, so that it is only about 30% efficient. But the body can easily compensate for that, in most people, by making more of the enzyme.

Some of those 9% who are homozygous for C677T may benefit from taking MTHF (also known as methylfolate) supplements. There is no need for them to take methylcobalamin because, as shown in the section above, it cannot be used in the hCys reaction unless MTHF is present.

Cyanocobalamin and the production of cyanide

Some people say that cyanocobalamin is no good because cyanide is produced. This is true, but the amount of cyanide is miniscule. One 1000 mcg dose of cyanocobalamin can produce the same amount of cyanide as you can produce from 7 apple seeds.

Disadvantages of methylcobalamin

Methylcobalamin is less stable than, more expensive than and more difficult to obtain in injectable form than either cyanocobalamin or hydroxocobalamin. There are also many, admittedly anecdotal, reports of some people suffering adverse effects from injecting methylcobalamin, whilst they are fine with cyanocobalamin and/or hydroxocobalamin.