The Blue People of Troublesome Creek

Background

The physical sciences are well-resourced in terms of ideas for demonstrations which can be used to support teaching and learning in the classroom [1-5]. Ramette [6] introduced the phrase 'exocharmic reactions' to describe reactions and demonstrations, particularly those in chemistry, which fascinate, allure or delight the observer. Despite their undoubted value as pedagogic aids, collections of demonstrations for use in biology teaching are not widely available. One might argue, therefore, that we need some exocharmic demonstrations for biology. Whilst the example that follows is not new, a minor tweak to the standard experimental conditions used means that we have produced a 'nice' demonstration to support delivery of the biology curriculum.

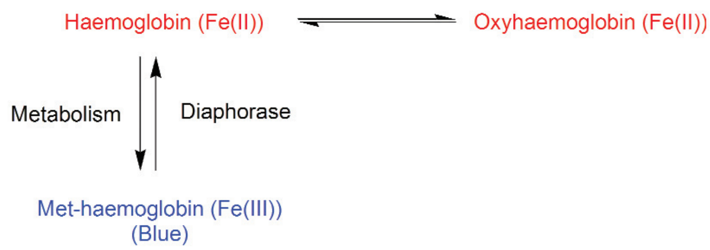
In the early part of the 19th century (1820) a French migrant, Martin Fugate, settled in a small hamlet called Troublesome Creek in Kentucky and married a local woman, Elizabeth Smith. Not much is known about their lives before they met but after their marriage they produced seven children and somewhat remarkably, and not a little worryingly, four of these children had blue skin at birth. As we will see later the affected children were suffering from a recessive disorder which led to a build-up of *methaemoglobin* which is itself blue in colour. One can only begin to imagine the social challenges faced by the family under such circumstances. What is clear is that as a result of their condition, the family was shunned by society and over time this led to a number of consanguineous marriages/ relationships (mainly at the cousin to cousin level although it is reported that one of the four 'blue children' married his maternal aunt) with the result that the disorder was confined to a few families.

What are the consequences?

Under normal circumstances the iron atom in haemoglobin (Hb) is in the Fe[II] state. Under those conditions Hb is able to transport both oxygen and carbon dioxide. Oxidation of the Fe[II] to Fe[III], through normal metabolic processes which happen in each and everyone of us, leads to the formation of methaemoglobin (MetHb) which, as stated above, is blue in colour. Accumulation of MetHb leads to a gradual increase in 'blueness' which is most noticeable in the skin and extremities. MetHb is unable to transport oxygen and unless reduction back to Hb occurs, a number of problems arise. Sufferers of the condition are often chronically anaemic since they will have a need to continually replace MetHb with newly synthesised Hb. Additionally, the reduced capacity to transport oxygen around the body may lead to excessive fatigue and lethargy. It is probable that those with the condition would have found physical activity difficult and this may have led to a reduction in income in what would have been difficult financial times.

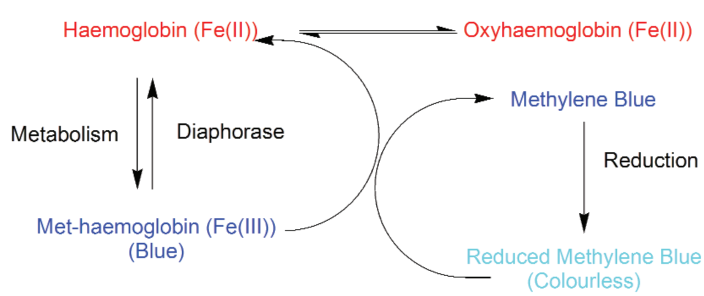
Why is the skin blue?

In the overwhelming majority of people the enzyme *diaphorase* is able to reduce the iron in MetHb to regenerate Hb. The Blue People of Troublesome Creek suffer from a recessive genetic disorder characterised by a failure of diaphorase production and/or its function. The condition leads to the accumulation of MetHb with consequent blue coloration of the skin. A word of caution - there are a number of websites which purport to show photographs of the Blue People of Troublesome Creek but one needs to be cautious since the first ever recorded colour photograph was not taken until 1861 (see http://en.wikipedia.org/wiki/Color_photography). The schematic below summarises the metabolic processes in play:



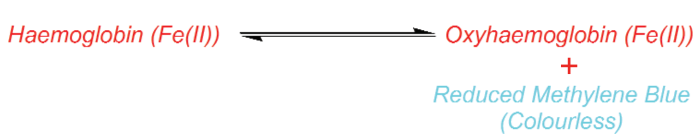
How is the condition treated?

In the 1960s Madison Cawein, a haematologist at the University of Kentucky, recognised the cause of the condition and decided to offer treatment through injections of methylene blue (MB). There is, of course, something wonderfully counter-intuitive about using a blue 'medicine' to treat a blue condition. The rationale behind the treatment is that to reduce the MetHb requires an electron donor. MB, when ingested into the body, is rapidly converted to a reduced form. This reduced form of MB, which is colourless, can take the place of diaphorase and convert MetHb back to Hb and as a result of that process the MB is oxidised back to its blue form. The MB is then, once more, reduced and is available for reaction with MetHb. Thus:



For each oxidation/reduction cycle of a MB molecule one MetHb molecule is converted to Hb. Once all the MetHb has been removed we finish up with a situation in which the following are present:

Excretion of reduced MB through the urine results in its reaction



with oxygen thereby re-forming oxidised MB. Consequently the urine of those treated turns blue on exposure to the atmosphere - a major side-effect of the treatment.

The Demonstration

The so-called blue bottle demonstration has been reported in the literature on a number of occasions [7-12]. In its 'standard' form a mixture of glucose and sodium hydroxide, in the presence of MB, is allowed to stand for a few minutes after which time the solution goes from deep blue to colourless. The chemical reactions taking place in the bottle need not concern us here but suffice to say that the MB is reduced to its colourless form. The blue bottle is often used in kinetic studies as well as in 'chemical shows' where audiences are often intrigued by the change in colour.

Some years ago Fenster *et al.* [10] suggested that the blue bottle was a good demonstration to use to describe the use of MB in the treatment of the Blue People. Typically one would prepare glucose and sodium hydroxide solutions both of which contained MB. At 'show-time' equal volumes of these solutions are mixed together and the colour change awaited. A minor problem of this approach is that the solution goes colourless rather than back to a pink/red colour as one might expect if Hb (in its Fe[II] state) was present. So, we set about making a minor adjustment to the experimental set-up such that the colour change is blue ➛ pink/red rather than blue ➛ colourless. The following stock solutions were prepared:

- glucose (0.24 mol dm^{-3}) in distilled water
- sodium hydroxide (1.0 mol dm^{-3}) in distilled water (CORROSIVE)
- methylene blue (2.7×10^{-2} mol dm^{-3}) in distilled water (Solid MB is HARMFUL if swallowed, if inhaled and in contact with skin. Severe eye IRRITANT.)
- Rose Bengal (1.0×10^{-2} mol dm^{-3}) in ethanol.

Into the lid of a Duran bottle (1 dm^3) place 4 drops of the Rose Bengal solution and allow the solvent to evaporate to dryness (at room temperature this may take several hours). Equal volumes (400 cm^3) of the glucose and sodium hydroxide solution are placed in beakers and 4 drops of the MB is added to both solutions. The contents of both beakers are poured into the empty Duran bottle and the lid treated with Rose Bengal is added. The bottle is shaken vigorously making sure that the Rose Bengal is washed from the lid. At this stage the solution will still appear blue in colour but over the next few minutes will change to a pink/red colour mimicking the colour changes described when MB is used to treat the Blue People of Troublesome Creek.

To complete the demonstration it is worth reminding your students that oxidised MB is blue in colour. Of course the Duran bottle now contains reduced MB and exposure to oxygen in the atmosphere will convert MB to its oxidised form (as happens during urination). So the final part of the demonstration is to pour (we recommend from a height of about 50 cm – be careful the solution also contains sodium hydroxide so you should avoid contact with your skin and wear indirect vent goggles) the red/pink solution into a clean beaker (1 dm^3). The solution during this process will turn blue – definitely exocharmic!

©Anne Beaumont

References

1. Shakhashiri, B.Z. (1983), *Chemical Demonstrations: A Handbook for Teachers of Chemistry - Volume 1*. University of Wisconsin Press, Madison.

2. Shakhashiri, B.Z. (1985), *Chemical Demonstrations: A Handbook for Teachers of Chemistry - Volume 2*. University of Wisconsin Press, Madison.

3. Shakhashiri, B.Z. (1989), *Chemical Demonstrations: A Handbook for Teachers of Chemistry - Volume 3*. University of Wisconsin Press, Madison.

4. Shakhashiri, B.Z. (1994), *Chemical Demonstrations: A Handbook for Teachers of Chemistry - Volume 4*. University of Wisconsin Press, Madison.

5. Taylor, C. (1988), *The Art and Science of Lecture Demonstration*. Adam Hilger/Institute of Physics Publishing Ltd., Bristol.

6. Ramette, R.W. (1980), Exocharmic reactions. *J. Chem. Ed.*, **57**, 68-69.

7. Adamcíková, L. and Ševcík (1998), The blue bottle experiment – simple demonstration of self-organization. *J. Chem. Ed.*, **75**, 1580.

8. Cook, A.G., Tolliver, R.M. and Williams, J.E. (1994), The blue bottle experiment revisited. How Blue? How Sweet? *J. Chem. Ed.*, **71**, 160-161.

9. Engerer, S.C. and Cook, A.G. (1999), The blue bottle reaction as a general chemistry experiment on reaction mechanisms. *J. Chem. Ed.*, **76**, 1519-1520.

10. Fenster, A.E., Harpp, D.N. and Schwarcz, J.A. (1988), A well-known chemical demonstration to illustrate an unusual medical mystery. *J. Chem. Ed.*, **65**, 621.

11. Vandaveer, IV W.R. and Mosher, M. (1997), The blue bottle revisited. *J. Chem. Ed.*, **74**, 402.

12. Wellman, W.E. and Noble, M.E. (2003), Greening the blue bottle. *J. Chem. Ed.*, **80**, 537-540.

Additional Resources

The Blue People of Troublesome Creek – an article by Cathy Trost based on a publication in Science in November 1982. http://www.rootsweb.ancestry.com/~kyperry3/Blue_Fugates_Troublesome_Creek.html (accessed March 10th 2009).

The Blue People of Troublesome Creek – a PowerPoint file giving background details and the reaction schematics in this article. Available at http://www-saps.plantsci.cam.ac.uk/docs/ppts/BluePeoplepb.ppt (accessed March 10th 2009)