10.12 Folate Deficiency & Toxicity

Folate deficiency is a vitamin deficiency that affects some Americans. The hallmark symptom of folate deficiency is megaloblastic (aka macrocytic) anemia. Megaloblastic anemia, as the name suggests, is characterized by large, nucleated (most red blood cells do not have a nucleus), immature red blood cells. This occurs because folate is needed for DNA synthesis; without it red blood cells are not able to divide properly\(^1\). As a result, fewer and poorer functioning red blood cells are produced that cannot carry oxygen as efficiently as normal red blood cells\(^2\).

A maternal folate deficiency can lead to neural tube defects in infants. The exact cause of neural tube defects is unknown, but folate supplementation has been shown to decrease the incidence of neural tube defects\(^3\). The most common of these neural tube defects is spina bifida (1 out 2500 babies born in the United States), which is a failure of the neural tube to close and the spinal cord and its fluid protrude out the infant's back, as shown below\(^4,5\).

![Spina Bifida](image)

Figure 10.121 Spina bifida\(^6\)

The neural tube closes 21-28 days after conception\(^1\), and with 50% of pregnancies estimated to be unplanned, many women aren't aware they are pregnant during this period\(^1,2\). Thus, it is recommended that women of childbearing age consume 400 ug of folic acid daily\(^1\). In addition, in 1998 the FDA mandated that all refined cereals and grains be fortified with 140 ug folic acid /100 grams of product\(^7\). As you can see below, spina bifida incidence rates have been declining in the United States since approximately 1995, before folic acid fortification began.
Figure 10.122 Spina bifida incidence rates 1992-2006

The following link is an interesting account of the history that led up to the folic acid fortification. It is debatable whether folic acid fortification was responsible for the decrease in spina bifida rates shown above.

**Web Link**

[Folic Acid Fortification: Fact and Folly](http://www.fda.gov/AboutFDA/WhatWeDo/History/ProductRegulation/SelectionsFromFDLIUpdateseriesonFDAHistory/ucm091883.htm)

Folate isn't toxic, but it can mask a vitamin B₁₂ deficiency and prevent its diagnosis. This effect will be discussed further in the vitamin B₁₂ deficiency section.

**References & Links**

8. http://www.cdc.gov/nchs/data/hestat/spine_anen_fig_1.png

**Link**

Folic Acid Fortification: Fact and Folly -
http://www.fda.gov/AboutFDA/WhatWeDo/History/ProductRegulation/SelectionsFromFDLIUpdateseriesonFDAHistory/ucm091883.htm