

NODDING HEAD DISEASE

A mysterious new disease is afflicting children in Uganda, Sudan and Tanzania and has left health workers baffled. It affects a tight age range of 5 to 15 years. Children begin to have head nodding which occurs in clusters and is often precipitated by food and cold weather. Affected children continue to slowly deteriorate, with progressive cognitive decline and emaciation. They will often have frank seizures. No one has recovered so far.

How do we look at a brand new disease? Is it infectious? Are toxins involved? Why is there such strong temporal and geographic clustering of an unusual and unexplained syndrome, consistent with epilepsy? The CDC is assisting the South Sudan Ministry of Health with its ongoing investigations. Proposed etiologies include infections, nutritional, environmental, and psychogenic causes. Specific exposures evaluated in previous studies include munitions, measles, monkey meat, relief seeds, or relief food (e.g., lentils and sorghum). However all investigations have drawn a blank. A case control study by the CDC has shown a higher incidence of onchocerciasis, but the causal pathophysiologic mechanism is not clear, and some have concluded that the association is spurious. Although the cause of nodding syndrome remains unknown, the CDC has recommended mass ivermectin treatment for onchocerciasis and antiepileptic medication. But the jury is not out yet about who or what is the culprit of this new syndrome (*The Washington Post* 29 July, 2012, *MMWR* 27 Jan 2012).

FIRST MAN TO BE CURED OF AIDS?

Timothy Ray Brown also known as “The Berlin Patient” may go down in history as the first patient to be cured of AIDS. He was first diagnosed to have AIDS in 1995. In 2007 while living in Germany he underwent a stem cell transplant for AML. His donor had the CCR5 Δ32/Δ32 mutation. He has remained free of HIV and off antiretroviral drugs since then despite a relapse of AML requiring a second successful transplant. He has achieved immune reconstitution with adequate numbers of CD4 cells in blood and gut mucosa with donor cells, without any evidence of HIV virus replication. HIV RNA and DNA have not been detected in plasma and other tissues.

This single patient study has generated intense speculation and interest in both the academia and the hoi polloi. The key is considered to be the CCR5 Δ32/Δ32 mutation. The CCR5 gene codes for a protein which acts as a receptor for the HIV virus on CD4 cells. Tim Brown received stem cells from a donor who was homozygous for a mutation on the CCR5 gene which is known to confer immunity to primary infection and slow

disease progression in established HIV infection. This gene is present in 1% of Europeans and arose sometime in the middle ages and probably conferred some protection against the plague or small pox.

It is hard to prove with certainty that HIV has been fully eradicated from all its secret nooks and crannies. We are treading new ground and how long without symptoms and without drugs means cure is still to be defined. Stem cell therapy is invasive and expensive. Not all HIV-infected patients who can live long, healthy lives with the use of ART need it. Nor is it feasible to find HLA-matched donors with Δ32/Δ32 mutation for the majority of people. Yet this study, the first of its kind, provides a proof of concept for further evaluation of strategies in the conquest of this quintessentially elusive virus (*Blood* 2011;117:2791-9).

INNOVATION CRISIS IN DRUG RESEARCH

Two authoritative articles in the *BMJ* have slammed the pharmaceutical industries constant harping of the so called “innovation crisis in drug research”. The authors argue that telling “innovation crisis” stories to politicians and the press “serves as a ploy to attract a range of government protections from free market competition.” Stories that the pipeline for new drugs will soon dry up due to lack of government support are untenable. The number of new drugs which debut each year continue steadily at a long term average of 15 – 25 a year. On the down side independent reviews have clearly shown that 85-90% of all new drugs in the past 50 years have provided few benefits but considerable harm. Though the industry constantly harps at how much it devotes to develop new drugs, the truth is that most of the money goes in funding innumerable minor variations of a known drug which brings in a steady stream of profits. Heavy promotion of these drugs can account for up to 80% of a nation’s drug spending. According to an independent analysis, the 1.3% of revenues devoted to discovering new molecules compares with an estimated 25% spent on promotion, giving a ratio of basic research to marketing of 1:19.

So, what can be done to change the business model of the pharmaceutical industry to focus on more cost effective, safer medicines. The first step should be to stop approving so many new drugs of little therapeutic value. Drug manufacturers should have to show how their products compare to existing treatments before approval. Raising the evidence standards could also encourage manufacturers to concentrate on the development of new drugs in therapeutic areas with few or no alternatives (*BMJ news* 7 August 2012).

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