

Oxford scientists say hormone 'overdose' may affect seriousness of infections

**Tim Radford
Science Editor**

AN Oxford team may have answered one of the great riddles of infectious diseases: why some people are badly hit while others shrug the infection off.

It could be a genetic "overdose" of a hormone called tumour necrosis factor (TNF) — one of the defence chemicals

of the immune system known to destroy cancerous cells.

Bill McGuire and others, of the Medical Research Council's Institute of Molecular Medicine, based in Oxford and Gambia, studied the impact of malaria on 1,000 Gambian children. They report in Nature today that those with the worst form, cerebral malaria, had a genetic tendency to produce high levels of TNF, and these were seven times as likely to

die or suffer brain damage.

The culprit appears to be a particular variant of the TNF gene, and affects only those who inherit a copy of the variant from each parent. Although malarial infection is common in West Africa, only a small proportion of children suffer from the cerebral form.

"TNF is a normal part of self defence," said Dr McGuire. "It activates the immune system. There are various ways in

which this molecule can help you fight malaria, and there are side effects such as body aches and fevers which are the common symptoms. It's only when you produce far too much that you tend to get the uncommon but fatal complications.

The same double-edged sword may be at work in other microbial infections. Dr McGuire believes that TNF may have a role in wildly different responses to tuberculosis

— which infects almost one third of the globe — and leprosy, which infects 20 million worldwide.

"Some people clear the TB bacillus quite quickly and other people go on to have a wasting illness," he said.

"Leprosy is the classic example. The same bacillus can affect people in very different ways. Any infectious disease is always a battle between the parasite and the host."

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