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Blood disease protects against malaria in an unexpected way

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Children with an inherited blood disorder called alpha thalassemia make unusually small red blood cells that mostly cause a mild form of anemia. Now, researchers have discovered that this disorder has a benefit—it can protect children against one of the world's greatest killers, malaria, according to a new study.

"We made the surprising finding that packaging your hemoglobin in smaller amounts in more cells is an advantage against malaria," says Karen Day, Ph.D., Professor and Chairman of the Department of Medical Parasitology at NYU School of Medicine, who led the research with colleagues at the University of Oxford. Hemoglobin is the oxygen-carrying protein in red blood cells.

The new research shows how children with a mild form of alpha thalassemia are protected against life-threatening malarial anemia. The study, published in the March issue of the journal *PLoS Medicine*, proposes an answer to a biological puzzle that first emerged more than 50 years ago.

Some 800 children living in Papua, New Guinea, participated in the study. Malaria is endemic in Papua New Guinea and 68 percent of children living there have alpha thalassemia. Dr. Day and her then-Ph D. student Freya J.I. Fowkes, and colleagues from the University of Oxford, Papua New Guinea Institute of Medical Research, and Swansea University, show that an attack of severe malaria causes the loss of one-third to one-half of the total number of red blood cells, which number in

the trillions per liter of blood. Children with mild alpha thalassemia tolerated this massive loss because they started out with 10 to 20 percent more red blood cells than unaffected children.

“It is really remarkable and so simple. Children with alpha thalassemia have adapted to the loss of red blood cells associated with malarial disease by making more of these cells with less hemoglobin,” says Dr. Day. “So, these children do better because they end up with more hemoglobin overall when they have a malaria attack compared to normal children,” says Dr. Day.

Malaria has been a scourge for thousands of years. The parasite causing the disease spends part of its life inside human red blood cells, which are eventually destroyed. Severe anemia occurs in some children with malaria when blood cell loss leads to hemoglobin levels of less than 50 grams per liter.

Malaria afflicts hundreds of millions of people, causing up to 2 million deaths every year in Africa and Asia. Many of its victims are young children. In regions of the world where malaria is endemic, mutations have arisen in human populations that allow people to survive. Sickle cell trait, for example, protects against malaria.

Nearly sixty years ago the renowned evolutionary biologist J.B.S.Haldane postulated that the thalassemias were common in human populations because they protected against malaria. Alpha thalassemia is common in Asia, the Mediterranean and Melanesia where malaria is or was prevalent. In the mid 1990s researchers working on the north coast of Papua New Guinea proved that children with mild alpha thalassemia, who inherit mutations in the “alpha” part of hemoglobin genes from each parent, were protected against malaria. These children were 60 percent less likely to get severe malarial anemia than normal children, however the mechanism of such protection was unclear.

Dr. Day and colleagues based their new study on this same population of children. “We are proposing an unexpected mechanism of protection against severe malarial anemia” says Dr. Day. “We show that alpha thalassemia is giving the child a hematological advantage by making more red blood cells.

According to the National Human Genome Research Institute, part of the National Institutes of Health, most individuals with alpha thalassemia have milder forms of the disease, with varying degrees of anemia. The most severe form of alpha thalassemia, which mainly affects individuals of Southeast Asian, Chinese and Filipino ancestry, results in fetal or newborn death.

Source: New York University Medical Center