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New Model Promises New Treatment Modalities for **Malaria**

By Karla Gale

NEW YORK (Reuters Health) Nov 24 - The new field of "microfluidics" may enable heretofore impossible discovery of agents to treat **malaria**, according to a report in the early edition of the Proceedings of the National Academy of Sciences, published online November 24.

Previous research was hampered by having to study infected erythrocytes in bulk, or isolated cells where only one parameter at a time could be measured, co-author Dr. Pradipsinh K. Rathod told Reuters Health.

Dr. Rathod's group at the University of Washington in Seattle used electron beams to etch channels into a silicone-based elastomer to mimic capillaries of 2 to 8 micrometers in diameter, allowing them to examine the mechanical aspects of **malaria** infection.

They found that uninfected erythrocytes did not adhere to channel walls, and could easily traverse 2-micrometer constrictions.

However, RBCs isolated at different stages of infection lost their flexibility and their membranes became more rigid, and after squeezing through the narrow channels, the ability to recover their normal shape was delayed. These characteristics worsened as erythrocytes progressed through stages of infection, so that schizonts could not pass through channels of less than 8 micrometer width.

According to co-investigator Dr. Daniel T. **Chiu**, the altered deformability after parasitic infection seems to be due to alterations in the erythrocyte cytoskeleton and membrane composition.

The group also found that normal RBCs are pliable enough to squeeze through parasitized cells clumped together at the mouth of a blocked capillary, thus explaining the ability of blood transfusions to alleviate the effects of severe **malaria**.

To recapitulate the microenvironment in the spleen and examine the mechanics behind cell "pitting," in which parasites are removed from infected cells and the cells reenter the circulation, they generated channels of 2 micrometer.

This phenomenon was previously attributed to macrophages "feeding" on the infected cells, Dr. Rathod explained. In their model, they observed that the process is mechanical, with the more normal proximal portion of a cell passing through the restriction, whereas the parasitized distal part remains in the upstream portion of the channel. The membrane stretches until

it ruptures, allowing the normal part of the cell to return to circulation.

"We hope to use these types of capillary-like structures for high throughput assays of drugs," Dr. Rathod said. "We also can model more complex, and thus more relevant, systems in which macrophages and molecular receptors are introduced."

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