

# This Week's Citation Classic®

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Goodwin L. G. The pathology of African trypanosomiasis. *Trans. Roy. Soc. Trop. Med. Hyg.* 64:797-817, 1970.  
[Nuffield Institute of Comparative Medicine, Zoological Society of London, England]

Trypanosomes, by changing the structure of their surface coats, can evade the immune responses of their hosts in a succession of different antigenic variants. They eventually render the host incapable of reacting to antigens, although they stimulate a vast expansion of the mononuclear cell series and the production of large amounts of antibody. They also cause profound alterations in biochemistry and histopathological changes in the tissues of the host. [The *SC*® indicates that this paper has been cited in over 105 publications.]

## Complexities of Trypanosome Infections

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From 1939 to 1963 I worked at the Wellcome Laboratories of Tropical Medicine on the development of new drugs for the treatment of tropical diseases caused by protozoa and helminths. When promising new compounds had been selected from the large number screened for activity against infections in laboratory animals, I had the good fortune to be able to take them for clinical trial overseas.

My first trip was in 1951, to try some rather toxic new phenanthridinium derivatives on cattle trypanosomiasis in Nigeria—and the success and efficiency of trypanosomes as parasites fascinated me. In 1964 I moved to the London Zoo to direct a new Institute of Comparative Medicine, and this gave me the opportunity to look more closely into the pathology caused by African trypanosomes. I had colleagues with a wide range of knowledge and skills—Christine Hawkey (haematology),

George du Boulay (radiology), Peter Boreham (pharmacology), and Alister Voller (immunology).

We used many approaches to find out how trypanosomes damage their hosts. It was already known that successive waves of parasitaemia are caused by antigenically distinct variants that arise, one after the other, as each is suppressed by the host's immune response. We showed that the infection elicits the production of vast numbers of mononuclear cells and masses of immunoglobulin—most of it nonspecific. In the end, the host fails to respond to other antigens such as sheep erythrocytes—no doubt the reason human sleeping sickness patients often die of concurrent bacterial infections.

My first training was in pharmacology, and the discovery that vasoactive kinins were liberated during the infection was intriguing. We had excellent X-ray facilities and demonstrated that vasoconstriction occurred in the ears of infected rabbits. By injecting india ink, we showed that hosts of macrophages adhered to the walls of capillaries and venules and obstructed blood flow. We used implanted plastic "hair curlers" to collect tissue fluid for analysis—there were large increases in pyruvate, cholesterol, and enzymes released from degenerating muscle and collagen—and we used implanted chambers in rabbits' ears to study vascular and connective tissue lesions by microscopy.

The 1970 paper was a review of past and ongoing work at the laboratory and was an attempt to coordinate and explain the complex effects of trypanosome infections.

Since then a great deal more has been learned of the way in which trypanosomes, by transferring a gene to a special site at the end of a chromosome, can change their glycoprotein surface coats, and the expansion of the mononuclear cell population has been shown to be stimulated by the release of lymphokines.<sup>1</sup> But little more has been done with kinins, and there have been few recent histopathological studies. As Brian M. Greenwood says: "Such studies should be of interest now that a great deal more is known about the immunological importance of pathological changes in various parts of the lymphoid system."<sup>2</sup>

1. Greenwood B M & Whittle H C. The pathogenesis of sleeping sickness. *Trans. Roy. Soc. Trop. Med. Hyg.* 74:716-25, 1980. (Cited 20 times.)
2. Greenwood B M. African trypanosomiasis. (Weatherall D J, Ledingham J G G & Warrell D A, eds.) *Oxford textbook of medicine*. Oxford, England: Oxford University Press, 1987. Vol. 1. p. 5.515-5.520.

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