branch *D. limbata* biosynthesizes polypeptide (1), which constitutes its chemical defense and is stored in the mantle. Thus the ability of a nudibranch to elaborate its chemical defense has been demonstrated. *Dendrodois limbata* also synthesizes the mixture of sesquiterpenoid esters (2) found in the digestive glands. We believe that these esters should be regarded as products of further metabolism of polypodial as a result of a detoxication process. Polypodial is a reactive molecule that readily interacts with NH$_2$ groups (16) and therefore could be toxic for *D. limbata* itself if stored for a long time. When the animal is molested, the compound is secreted through the skin. The esters (2), which are found into the hepatopancreas only, could represent the normal excretory metabolites of polypodial.

Guido Cimino
Salvatore De Rosa
Salvatore De Stefano
Guido Sodano
Guido Villani
Istituto per la Chimica di Molecole di Interesse Biologico,
Consiglio Nazionale delle Ricerche,
Arco Felice, Napoli, Italy

Rheumatoid Factors and Chagas’ Disease

Clarkson and Mellow (1) report that they found antibodies with rheumatoid factor properties in the serum of lactating rats. They point out that such immunoglobulin “accounts for the unusual resistance of previously uninfected lactating rats and their sucking pups to infection with *T. lewisi,*” and that “a similar rheumatoid factor . . . which is induced late in the usual course of infection with *T. lewisi* in nonlactating rats, amplifies an earlier IgG response and terminates the infection.” They then draw a parallel between *Trypanosoma lewisi* and *T. cruzi* infections and suggest that “it might be possible to treat Chagas’ disease by temporarily inducing the production of rheumatoid factor.” Although the results of their experiments are interesting, I do not agree with certain aspects of their conclusions and I offer the following comments:

In early work with my colleagues (2) it was shown that humans infected with *T. cruzi* (Chagas’ disease) produce rheumatoid factor-like antibodies. Such factors are highly reactive with heterologous γ-globulin (3) and are demonstrable with the Waaler-Rose reaction (4); they are composed of immunoglobulin M (IgM) and are less responsive to human γ-globulin (3) prepared for the Singer and Plotz test (5). High titers of these rheumatoid factors were found in the serum of 95 percent of patients (infants, children, and adults) from the time of clinical onset (acute phase) of the disease to about 1 year (3). However, these factors were also found, intermittently, in 25 percent of patients with chronic Chagas’ disease (3). Such factors were found in patients with or without evident clinical lesions. These findings suggest that there is no correlation between the presence of rheumatoid factor and the course of infection in Chagas’ disease, and that IgM therefore plays a marginal role in modulating *T. cruzi* infections.

Although it is possible that the rheumatoid factors produced during Chagas’ disease are a natural protective response of the host to *T. cruzi,* it is also possible that these factors, because of their reactivity with γ-globulin, are autoantibodies. There is evidence that several tissue lesions in Chagas’ disease result from humoral and cellular autoimmune reactions (3, 6).

It seems unlikely, therefore, that the rheumatoid factors will be useful in the treatment of Chagas’ disease. For adequate treatment of this disease we still need an effective, nontoxic drug that will kill the parasite and some form of therapy to suppress the major autoimmune mechanisms that produce the lesions of Chagas’ disease.

HUMBERTO R. A. CABRAL
Instituto de Biologia Celular,
Facultad de Ciencias Medicas,
Universidad Nacional de Cordoba,
C. Postal 362, 5000 Cordoba, Argentina

References
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Cabrál (1) raises doubt about the possible extension of our findings (2) with *Trypanosoma lewisi* in rats to *T. cruzi* in humans. Although we considered this possibility only as a hypothesis to guide future research, there is other evidence that implicates a positive role for rheumatoid factors (RF’s) in *Trypanosoma* infections as well as in autoimmune disease.

Cabrál notes that RF appears in the serum of most patients with Chagas’ disease, generally before the development of a complement fixation titer (CFT), and states that RF is not correlated with protection. However, a negative CFT does not imply absence of parasite-specific immunoglobulin G (IgG). Also rheumatoid factors have a broad range of potential epitope specificities; an immunoglobulin M (IgM) that is specific for one epitope on a particular IgG subclass may be protective, whereas another RF, although generally reactive with bound or aggregated IgG, may not be protective. An analogy can be made to the overall immunoglobulin response to *T. cruzi* and many other infectious agents. With rare exceptions, all infected animals show an increase in serum immunoglobulins whether they resist or succumb to the disease. If one did not know that the specificity of these immu-
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HR Cabral

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