organisms or cell walls in *Rag-1* knockout mice, which lack mature T and B cells, led to significant myelin breakdown early during infection, comparable to the level observed in wild-type mice. From this, they conclude that *M. leprae*–induced demyelination can occur in the absence of immune cells.

These findings, however, do not explain two major clinical observations in leprosy. First, it is well known that nerve damage in leprosy occurs particularly during (upgrading) type-1 reactions. Type-1 leprosy reactions are idiopathic episodes of strongly increased inflammation and cell-mediated immune reactivity and are often accompanied by acute inflammation of peripheral nerves. The latter complication frequently leads to extensive and irreversible nerve damage. The treatment of choice is rapid administration of immunosuppressive drugs to prevent further nerve damage (*1*).

Second, although patients with lepromatous leprosy display demyelination and nerve damage, these processes are chronic and relatively slow, despite the presence of high bacillary indices. Thus, in the absence of an adequate cellular immune response, symptomatic neurodegeneration progresses relatively slowly, despite the abundant presence of *M. leprae* organisms.

These combined clinical and epidemiological data suggest that inflammatory immune reactions play an important role in leprosy nerve damage and that the mere presence of *M. leprae* itself does not explain the full phenotype of leprosy nerve damage. Indeed, inflammatory responses seem to be needed for the complete manifestation of demyelination and associated neurological symptoms in other neurodegenerative diseases, as Rambukkana *et al.* point out. In my view, this likely applies also to leprosy: During a first and early phase of *M. leprae*–specific targeting of peripheral nerves, contact-dependent myelin breakdown takes place, and this may continue to progress further. During episodes of enhanced immunity and inflammation, acute and extensive additional nerve damage can take place, to which cytokines and immune effector cells contribute (*2*, *3*), although the precise mechanisms involved remain to be elucidated.

Thus, in my view, the human immune response plays a significant role in the full manifestation of leprosy neuritis and nerve damage. It is important to empasize this point, given its implications for the effective treatment and management of nerve damage in leprosy control.

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Response

IT IS KNOWN THAT ALMOST ALL CLINICAL features of leprosy are associated with immune responses (*1*), but we know nothing about the early events, preclinical stage, and associated pathology in nerve injury. It is impossible to explain all features of a complex spectral disease like leprosy in one paper. Our report explains one aspect of this complex pathology, the early consequence of *M. leprae* interaction with myelinating Schwann cells.

The key message of our report is that demyelination is an early step in nerve injury after the attachment of *M. leprae* and its components to myelinated Schwann cells (*2*). It certainly does not explain the immune-mediated clinical features of leprosy; rather, it is a model system to study the molecular basis for early nerve damage. In the absence of immune cells, *M. leprae* attachment to Schwann cell-axon units, the earliest interaction of the invading pathogen (*3*), results in significant demyelination. Such myelin damage could set forth the foundation to recruit immune cells in later infection. We neither concluded nor stated our finding as the major mechanism of nerve damage in leprosy. In fact, we stated that an immune response is needed for the complete manifestation of nerve damage in leprosy and other neurodegenerative diseases. Because the clinical manifestation of nerve injury, mainly due to inflammatory responses, occurs years after a slow infectious process, it is obvious that other events are occurring before the immune system comes into play. In fact, we know nothing about the early or preclinical stage of leprosy (certainly not after 72 hours postexposure, as in our study).

Thus, in early *M. leprae* infection, mechanism(s) other than immune responses are certainly involved in nerve injury. Because the Schwann cell is a privileged site for *M. leprae* that eludes surveillance by immune cells (*3*), we concluded that such non–immune-mediated mechanisms may play critical roles in nerve damage in the very early stage of the infectious process, although it may not be able to manifest clinically.

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Letters to the Editor

Letters (~300 words) discuss material published in *Science* in the previous 6 months or issues of general interest. They can be submitted by e-mail (science_letters@aaas.org), the Web (www.letter2science.org), or regular mail (1200 New York Ave., NW, Washington, DC 20005, USA). Letters are not acknowledged upon receipt, nor are authors generally consulted before publication. Whether published in full or in part, letters are subject to editing for clarity and space.

Mistaken Identity

MARTIN DELANEY'S REVIEW OF JOHN Crewdson's book *Science Fictions* ("Double jeopardy for Gallo," Books *et al.*, 31 May, p. 1615) is excellent and to the point. However, I am somewhat confused by the photograph picturing Robert Gallo and Luc Montagnier. The accompanying caption identifies Gallo at the left and Montagnier at the right. They are now good friends, but did they really exchange identities?

EDWARD DE MAEYER

The correct caption: Montagnier (left) and Gallo (right) embrace after being honored at a 2000 ceremony in Spain for identifying HIV.

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The Ups and Downs of Global Research Centers

HERE, WE PRESENT AN ANALYSIS OF THE changing performance of the largest "research centers" of the world. Of the total 2,790,179 papers listed by the Science Citation Index (SCI) for the period 1996–98, 38.3% have at least one author from the top 40 research centers. This formidable concentration pattern of research output is reinforced in 1999–2001, with 39.6% of the 2,929,977 papers associated with the world's 40 largest research centers.

Here, we define a center as a "greater