“active infection” by possible cofactors. In the case of herpesviruses, because of their ubiquitous nature, conventional serological methods are inadequate to document reactivation or active reinfection. In fact, the demonstration of an intact humoral immune response may be an implicit index of less advanced immunodeficiency, since antibody production by B lymphocytes is a helper (CD4) T-cell-dependent activity. This caveat can help in interpreting the inverse correlation found by some workers between anti-HHV-6 IgG titres and progression of HIV infection. With respect to concerns about the pathogenic role of HHV-6 in specific organ disease, we concur that it may still be premature to conclude that HHV-6 is a bona fide aetiological agent of pneumonitis or other disorders. Establishing an aetiological link between a ubiquitous agent such as HHV-6 and disease, particularly in the immunocompromised patient, may need multiple diagnostic approaches simultaneously. Only controlled studies of virus replication in longitudinally followed patients will help to define the pathology of HHV-6 infection.

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Proposed classification of herpes zoster pain

Sir—The efficacy of antiviral drugs in the treatment of pain associated with acute herpes zoster, and the rapidly enlarging repertoire of non-traditional analgesics for postherpetic neuralgia1 highlight the importance of pain assessment in the evaluation of treatments for herpes zoster. The duration of pain from herpes zoster is variable. At some point, persistent pain is diagnosed as postherpetic neuralgia. The confusing nature of this diagnosis is apparent in the published definitions of postherpetic neuralgia, which have ranged from pain that persists beyond crusting of the lesions to pain that persists beyond 6 months.2 In the absence of a consensus, the definition of postherpetic neuralgia has been considered arbitrary and it has been suggested that herpes zoster pain be treated as a continuum.3 This is unfortunate, because a uniform approach to the classification of herpetic pain would be desirable in research on treatment outcome and in studies that assess risk factors for postherpetic neuralgia.4

An acute herpes zoster infection usually heals within 4 weeks. Therefore, acute herpetic neuralgia is most appropriately applied to pain that occurs during the 30 days after the onset of the characteristic exanthem (which can be dated more accurately than onset of the first symptom, often pain or dysesthesia). The International Association for the Study of Pain (IASP) has described chronic pain as pain that persists beyond the normal time of healing, and has considered 3 months as the “most convenient point of division between acute and chronic pain”.5 Following this convention, we propose that the term postherpetic neuralgia be used to describe pain that persists more than 3 months after the end of the acute period (or 4 months after onset). This definition is consistent with most of the clinical trials that have been carried out for this condition.6

Many patients have pain that persists beyond the acute period, but resolves within 3 months. This pain does not fulfill the IASP criteria for chronic pain, and we propose the label subacute herpetic neuralgia to describe it. By clearly distinguishing subacute herpes zoster pain from acute and chronic herpes zoster pain, this definition will make it possible to determine whether the characteristics of persistent, but ultimately transitory, pain correspond to those of postherpetic neuralgia. Various methods are available for assessing the severity and quality of pain, as well as the disability that often accompanies it. Interpretation of these data across studies will be greatly facilitated by use of a classification that clearly distinguishes acute, subacute, and chronic herpetic neuralgia. This classification has the potential to provide greater uniformity in research on this common infection. Supported by National Institute of Neurological Disorders and Stroke grant RO1-NS-30714 to RHD.

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Complete remission of metastatic colorectal cancer: a pitfall in a multidrug resistance reversal trial

Sir—Drug resistance is considered to be an important cause of chemotherapy failure. One of the most extensively studied types of drug resistance is P-glycoprotein (Pgp) mediated multidrug resistance (MDR).4 MDR is an in-vitro phenomenon of cancer cells becoming cross resistant to a broad variety of structurally unrelated, natural product, anticancer drugs, after having been exposed to only one of them. Pgp is a plasma membrane protein of 170–180 kDa, encoded by the MDR1 gene, and acts as an energy-dependent drug efflux pump, thereby decreasing the intracellular anticancer drug concentration. Of interest is that MDR can be reversed both in vitro and in vivo by several resistance modifying agents. One of these is bepridil, a calcium channel blocker.5 Colorectal mucosa and most colorectal cancers express high concentrations of MDR1, and this may contribute to the insensitivity of colorectal cancer to natural product anticancer drugs such as vinblastine.6 We investigated the possibility of overcoming MDR in patients with advanced colorectal cancer by combining bepridil with vinblastine (5 mg/m²).7

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