Sir,

re: Interferon Preparations and Contaminating Endotoxin

Recent papers (1, 2, 3) have outlined some doubts associated with the variable responses in the results of interferon therapy of malignancies. Unknown contaminants have been indicated (4) in these different and ambiguous findings. We would like to suggest the endotoxic lipopolysaccharide as an unsuspected candidate. In fact, on account of its ubiquitous diffusion and physico-chemical stability, endotoxin is the contaminant that most concerns the producers of biological products (5). We (6), like others (7, 8), have demonstrated that some interferon preparations (IFNα) are charged with different amounts of endotoxin: contaminating endotoxin may be confused with the effect of the material in which it is present, and could alter the results of experimental research and clinical observation. In fact, the myriad of biological activities of endotoxin includes both a beneficial effect on the tumor area (9) and an increase in interferon production (10). However, in studies of this sort it is most important to establish the level of apparent contamination in preparations so that one can compare this level with known levels of endotoxin in similar experimental models; in this way one can be sure of the significance of one's findings. In view of this, endotoxin content in processed materials should be either tested by investigators or certified by producers before use. In this way the Limulus lysate gelation is extensively used as an *in vitro* correlation of endotoxin potential (11). However, endotoxin is only one of the possible contaminants involved in the variable activity of interferon preparations: detailed investigations will be necessary to determine the profile and exact role of other representatives of this still obscure catalogue.

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Sir,

re: Toxic Shock Syndrome: Interaction of Endotoxin and Staphylococcal Toxins

In the last few months *Begdoll* et al. (1) have identified a new staphylococcal enterotoxin associated with Toxic Shock Syndrome (TSS). In the same time, a recent paper by *Schlievert* (2) has described a new staphylococcal pyrogenic exotoxin involved in TSS. We should like to suggest another possible mechanism in the ambiguous pathogenetic mechanism of TSS, proposed by us in 1979 (3). Since the conventional staphylococcal enterotoxin (4) and a new staphylococcal exotoxin (2) from *Staphylococcus aureus* isolates in TSS enhance host susceptibility to lethal shock and increase the tissue damage by endotoxin (which gains entrance to the systemic circulation as a consequence of the endothelial injury caused by staphylococcal toxic products [4]), we suggest – at least in the cases of TSS where *S. aureus* was isolated – both a direct action of these toxins and an indirect mediation by endotoxin. In fact, many manifestations described in TSS (e. g. high fever, profound hypotension, propensity to acute renal failure, liver and central nervous system abnormalities, thrombocytopenia and/or coagulative disorders) are characteristic of endotoxin responses. Furthermore, there is accumulating evidence that many biological effects of endotoxin are mediated by prostaglandins (Prostaglandin involvement in TSS has been proposed by *Oskowitz* [5]).

However, without endotoxin assay, as performed in experiments with staphylococcal enterotoxin (4), one cannot assume this to be true.

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