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Anonymous anti-HIV agent

Ever since Robert Gallo and his colleagues reported (*Nature* **375**, 64; 1995) that crude, urine derived preparations of the human pregnancy hormone chorionic gonadotrophin (hCG) inhibit the growth of Kaposi's sarcoma (KS) cell lines and cause regression of KS lesions in mice, the race has been on to discover the mechanism of this action and whether hCG might be effective in the clinic.

The first task was to clean up the crude hCG preparations and confirm that the anti-KS activity remained. Taking it one step further, Albibi *et al.* showed that the important anti-KS activity resided in the beta-core fragment of the hormone (*AIDS* **11**, 713; 1997). Before long there was a flurry of small phase I clinical trials that variously introduced clinical grade hCG directly into the KS lesions, subcutaneously or systemically, showing that in about half of patients the treatment was successful. The exciting bonus was a gradual realization that some treated patients saw their HIV-1 plasma levels decline and their CD4 counts rise. Further work confirmed that hCG did indeed inhibit HIV-1 replication *in vivo*. More elaborate clinical trials were planned.

The first twist in the tail of this promising development came in December 1997 with the publication of a short report by Griffiths *et al.* (*Nature* **390**, 568) claiming that in fact an RNase contaminant of the hCG preparation was probably responsible for most of the anti-KS activity. Whereas at first glance this report seemed at odds with so much earlier work, on closer examination it appeared to make more sense: Griffiths and colleagues showed that the RNase was associated closely with the beta-core of hCG. They even speculated that "overall potent anti-KS activity of commercial hCG preparations might result from the combined effects of hCG and RNase activities."

With hindsight, this may have been an all too eager attempt to fit a square peg into a round hole—hindsight, because in this issue Gallo and colleagues show that the anti-KS and anti-HIV-1 activities belong to neither hCG nor RNase. Instead they ascribe these properties (and, in contrast to most chemotherapies, a pro-hematopoietic effect) to an unidentified urinary factor that they have dubbed HAF or hCG-associated factor.

This latest finding brings the story full circle. The original 1995 paper was prompted by a fortunate accident; while studying neoplastic KS cells in mice, Joseph Bryant, one of Gallo's collaborators, inadvertently assembled a mixed cage of male and female animals. Bryant was surprised to find that some of the mice failed to develop KS lesions. Closer examination revealed not only the mixed sexes but also that all the neoplastic-negative mice were female and pregnant. Assuming a pregnancy-related inhibitory effect at work, the researchers hastily reviewed the literature on early pregnancy hormones and found that hCG is very high in early human pregnancy. What they missed was that mice do not produce chorionic gonadotrophin!

Whatever it turns out to be, HAF holds much promise for treating KS, HIV-1 infection and Gallo and colleagues are working overtime to purify enough to identify the mysterious substance. This is not without problems—the only known source is first trimester human urine and it took 40 liters just to get this far.

Vaccines—no cause for concern

That vaccines may cause diseases distinct from those they are designed to prevent is not a new idea. Although the question of vaccine risks has been debated over the years, causal links have been difficult to establish, presumably because either they do not exist or the risk is so low as to be next to impossible to identify and investigate. Every now and again a study comes along that fans these embers of concern. Such a study was published in a recent issue of *The Lancet* (**351**, 637; 1998).

A London-based group saw 12 children referred with symptoms of autism and gastrointestinal disturbances. The alarm was raised when parents and physicians of eight these children reported that the child had received a mumps/measles/rubella triple vaccine between one and fourteen days before the first onset of symptoms. Although the authors of the article are careful not to claim a causal link, the suggestion that MMR vaccines might cause autism was enough to prompt a flurry of media attention.

Hats off to *The Lancet* for balancing this provocative report with a sober assessment of the data and its implications. In a commentary piece, Robert Chen and Frank DeStefano point out some obvious problems with the study—problems that must be pointed out every time a vaccine is implicated in such serious health problems. For example, with so many children receiving the MMR vaccine (more than half a million a year in the United Kingdom alone) it is inevitable that some coincidentally will also develop or acquire unconnected diseases around the time they are vaccinated. Any research group with a reputation for investigating such events will naturally attract such cases, and before one knows it one is reporting a series of patients who at first glance appear to reveal a frightening link between vaccination and disease.

All medical procedures carry a risk, and good surveillance is important. With vaccines it is paramount—not only because of the huge number of children involved but because vaccination is a communitybased intervention. In the long term it can be successful only when everyone or nearly everyone contributes to a resolve to beat the disease. Reports of vaccine-associated dangers, reliable or not, weaken that resolve and may, if left unchecked, do untold damage.