Preventing cervical cancer — a global issue

To the editor — Patricia Braly's News & Views[1] on a recent consensus report on cervical cancer addresses important issues but only from the perspective of more affluent countries. The incidence of cervical cancer is impressively high in the rest of the world with rates up to 64/100,000 women a year — almost nine times that of white North Americans. In sub-Saharan Africa alone, an estimated 53,000–130,000 women develop this malignancy each year. There is therefore a need for research with implications for treating this group of patients.

For example, there is compelling evidence that schistosomiasis, an infection that affects about 200 million people worldwide, contributes to the development of cancer in various organs such as the urinary bladder, liver and large intestine. A causal relationship between *S. haematobium* and bladder cancer has recently been acknowledged[2]. This parasite often invades genital organs, making female genital schistosomiasis (FGS) the most frequent complication of schistosomiasis haematobium[3]. An association between cervical schistosomiasis and cervical carcinoma has been suspected because the cervix is the most frequently affected genital site[3]. In Tanzania, 32 percent of women with cervical cancer had schistosome lesions at the cervix[4]. Coinfection with human papillomavirus (HPV) was not ruled out in these studies, but evidence exists that cervical cancer may develop in the absence of HPV infection in schistosomiasis endemic areas[5].

To date, no causal relationship between FGS and cervical cancer has been shown. However, if we assume that the pathogenesis of malignancy involves at least two distinct and sequential effects on the target cells — initiation and promotion — the impact of schistosome lesions at the cervix cannot be ruled out.

Initiatives concerned with the prevention of cervical cancer must be of a multidisciplinary nature, since regional biomedical and sociocultural determinants are of importance. It is pointless, if not cynical, to call for better screening and the development of an HPV vaccine for women lucky if they see a gynecologist once during their whole reproductive life and when risk factors other than HPV could play a dominant role.

1. Braly, P. Preventing cervical cancer. *Nature Med.* **2**, 749–751 (1996).
2. IARC Working Group on the Evaluation of Carcinogenic Risks to Humans. Schistosomes, liver flukes and *Helicobacter pylori*. *IARC (Int. Agency Res. Cancer) Monogr. Eval. Carcinog. Risks Hum.* **61** (1994).
3. Feldmeier, H., Poggensee, G., Krantz, I. & Helling-Giese, G. Female genital schistosomiasis: New challenges from a gender perspective. *Trop. Geogr. Med.* **47** (Suppl. 2), 2–15 (1995).
4. Moubayed, P., Lepère, J.-F., Mwakyoma & H., Neuvians, D. Carcinoma of the uterine cervix and schistosomiasis. *Int. J. Gynecol. Obstet.* **45**, 133–139 (1994).
5. Helling-Giese, G. *et al.* Female genital schistosomiasis: Relationship between gynaecological and histopathological findings. *Acta Trop.* (in the press).

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SIV and HIV prophylaxis

To the editor — We read with interest the recent report by Thomas Lehner and colleagues of protective mucosal immunity in macaques using a subunit SIV envelope and core protein vaccine[1]. Several injections of the vaccine were administered in alum and by different routes including the TILN route (via targeted iliac lymph nodes, which drain the genitorectal mucosa). Immunized and control monkeys were challenged with SIV by the rectal route. Control monkeys received no treatment before challenge. Specific secretory IgA was produced following immunization. SIV antigen-specific $CD8^+$ cytotoxic T cells were not found, as would be expected with this regimen. Complete or partial protection was achieved in all seven immunized recipients, and one of eight control monkeys resisted infection. There was no correlation between protection and specific secretory IgA levels at the mucosal sites, but protection was associated with significant increases in the iliac nodes of IgA antibody-secreting cells to the core antigen (presumably not possessing any viral infectivity-neutralizing activity), CD8 suppressor factor (SF) and the chemokines, RANTES and MIP-1β. The uninfected control monkey possessed CD8-SF activity. The authors suggest that the macaques may develop resistance to SIV infection by acquiring CD8-SF and β chemokines through some natural, possibly cross-reacting immunity. We believe this finding has important implications for HIV prophylaxis and/or therapy and wish to offer an interpretation of the data that may help this field to progress.

Activation and differentiation of naive $CD8^+$ T lymphocytes requires the antigen-presenting cells (APCs), often dendritic cells, to express both specific antigen (peptides bound to class I MHC molecules) and costimulator molecules. However, antigen-specific T cells previously activated and forming the pool of memory $CD8^+$ T lymphocytes can be converted to effector cells by interaction with APCs that express costimulator molecules and antigens of unrelated specificities[2]. We propose that injection of SIV antigen plus adjuvant by the TILN route activated APCs in the iliac node and that this in turn activated many cells in the memory $CD8^+$ T lymphocyte pool, which then secreted the suppressor factors and possibly had cytotoxic T-cell activity to the environmental antigens, but not to SIV. It is also of interest in this connection that injection of mice with type 1 interferons can cause proliferation of the $CD44^{hi}$ subset of $CD8^+$ T lymphocytes[3] (activated cells including the memory population).

This suggestion can be tested in the SIV/macaque model by vaccinating with a highly immunogenic but not necessarily related antigen plus adjuvant by the TILN route and challenging rectally with both SIV and the other antigen. If this experiment were successful, it would open the way to new approaches to control HIV.

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