

COMMENTARY

A RATIONAL BIOLOGIC BASIS FOR SAFE SEXUAL CONDUCT IN PREVENTING THE SPREAD OF AIDS

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AIDS (acquired immunodeficiency syndrome), ARC (AIDS related complex) and ARL (AIDS related lymphoma) are infectious diseases respectively manifesting lymphocyte hypoplasia with progressive depletion, hyperplasia and neoplasia induced by human immunodeficiency virus, type 1 (HIV-1) (1). AIDS, ARC and ARL are commonly spread within and between individuals by infected *emperipoletic* (inside roundabout wandering) small lymphocytes in blood, semen, colostrum or endocervical mucus (2). Normally in healthy humans, each of these secretions has $\sim 2 \times 10^{5-6}$ small migrant lymphocytes/ml (3,4). Such *emperipoletic* small lymphocytes, migrating randomly at velocities observed to be as fast as $40 \mu\text{M}/\text{min}$, serve as effective vectors for AIDS, ARC and ARL because they normally migrate through single layers of cells, such as endothelial cells and columnar epithelial cells forming the lining of the rectum and uterus (2). They normally migrate through the interstices, meninges and placenta, but do not normally migrate through stratified epithelial cells, such as superficial layers of skin, mouth and vagina (5). The *emperipoletic* lymphocytes are unique in that they actually enter other cells, wander about inside, sometimes undergo lysis therein or

induce lysis in other cells, or wander through without overt reaction (5,6).

Usually HIV-1 are demonstrated in tissue culture by showing retroviral or reverse transcriptase production after injecting concentrated peripheral blood mononuclear cells or lymph node specimens into established cultures of PHA-stimulated lymphocytes, usually with added interleukin-2. Despite prolific retroviral RNA production in large germinal center lymphocytes (8), encapsulated, mature HIV-1 virions have not been shown to form or shed from lymphocytes or monocytes in the body, and remain to be observed in human blood, semen, milk or in endocervical secretions. Such retroviruses can sometimes be cultured from cell-free supernates or filtrates added to such lymphocyte cultures (4), but it is not certain whether the infectious elements are actually intact virions, fragments of DNA containing integrated provirus released from fragile lymphocytes or monocytes during the handling or culturing of specimens, or non-integrated cytoplasmic viral RNA. Letvin et al (9) found that purified simian proviral DNA obtained from lymphocytes can transfect AIDS, when injected into monkeys. Because lymphocytes with or without CD4 surface receptors have never been shown to endocytose organic particles other than India ink or mycoplasma (5,10) but are prone to reutilize

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and re-express DNA derived from other migrant lymphocytes, (5) it would seem that the integrated HIV-1 provirus within *emperipoletic* lymphocytes is a more common means of human AIDS transfection than the mature encapsulated HIV-1 virion. Moreover, if encapsulated virions were the most common means of spread, we would still have to explain: how, in the absence of independent motility and lytic enzymes (apart from *reverse transcriptase* or *integrase*), such retrovirions actually penetrate living cells, especially cells lacking CD4 receptors and single layers of columnar cells which normally line the uterus and the gut?

Looking carefully at the numbers of small cytoplasm-poor *emperipoletic* lymphocytes normally found in human secretions (i.e., per milliliter of liquid samples) the averages we found were: semen— 2.5×10^6 ; colostrum— 1.3×10^6 ; saliva— 2.5×10^5 ; endocervical mucus— $1-3 \times 10^5$; cerebrospinal fluid— $1-5 \times 10^3$; urine— $0-2 \times 10^3$; sweat and tears—practically none (1,3). Anderson et al (4) found a median of $1-2 \times 10^5$ CD4+ lymphocytes per ml in semen before vasectomy; and $6.1 \times 10^3 \pm 2.6 \times 10^4$ T-lymphocytes (CD2, CD3) per ml in healthy vaginal pools. All counts varied greatly, depending on sampling times and methods (3,4). Looking at the barriers through which infected *emperipoletic* lymphocytes in various secretions are obliged to migrate to transfect AIDS, it appears that:

1. The transmission of AIDS via blood transfusions or sharing IV needles to inject drugs is extremely efficient, depending on the volumes shared, because each ml of blood normally contains $2-5 \times 10^6$ small migratory lymphocytes which need not migrate through epithelium or connective tissues to gain circulatory access.

2. The transmission of AIDS via semen to a receptive partner, male or female, during anal intercourse is relatively efficient because the rectum is lined entirely by a single layer of cells through which lymphocytes normally migrate with ease (1,2). Moreover, feces is alkaline and, thus, unlikely to interfere with

lymphocyte life-span or motility.

3. The male to female transmission of AIDS during conventional vaginal intercourse is less efficient, because the healthy vagina is normally lined by a thick stratified layer of epithelial cells through which lymphocytes do not normally migrate in the body (1,2), or in tissue culture (6). Therefore, like sperm which migrate much faster, “Trojan horse” seminal lymphocytes (11) must gain access through a relatively small opening into an alkaline uterine cervix lined by a single layer of columnar epithelial cells penetrable by *emperipoletic* lymphocytes (1,2).

4. The female to male transmission of AIDS during penile-vaginal intercourse is relatively inefficient because endocervical and vaginal secretions normally contain few lymphocytes compared with semen; and because the male penis and urethra are normally lined by a variably thick layer of stratified epithelial cells. However, if the endocervix is inflamed, or fresh blood oozes from the uterus during coitus, many more *emperipoletic* lymphocytes may be encountered. Moreover, if the penis is ulcerated by sexually transmitted diseases (STD), or the foreskin is thinned by lack of circumcision or balanitis, mutual risks multiply (12).

It should be added that AIDS transmission via spinal fluid, urine, sweat or tears has not been reported, possibly because such secretions are seldom shared; and they contain few lymphocytes. Salivary transmission is uncommon, possibly because the mouth is normally lined by thick stratified epithelium and most people don't bite others. Colostral spread is a major problem because the newborn gut is lined by a thin single layer of cells through which *emperipoletic* lymphocytes can migrate; and gastric acid production is minimal (5). Transplacental transmission is a vexing problem, possibly because *emperipoletic* lymphocytes of maternal and fetal origin normally exchange through the placenta (1,2).

HIV-provirus-infected small lymphocytes are commonly found in semen and cervical

mucus whereas mature cell-free HIV-1 virions remain to be demonstrated therein. Therefore, along with sexual abstinence or use of condoms, we should promote the use of currently available female barriers, such as vaginal diaphragms and cervical caps, which prevent the endocervical and uterine access of infected cells (7). Such female-choice barriers in common use for at least 50 years have not been found deleterious to women's health, particularly when used to prevent the intra-uterine migration of sperm. Moreover, we should urge the addition of detergents, such as nonoxynol-9, which in low, non-toxic concentrations reduce surface tension in fluids such that migratory cells, including lymphocytes and sperm cannot migrate effectively and, subsequently, gradually undergo lipid surface membrane deterioration (7). Such recommendations could provide life-saving for many young people at risk for AIDS and other cell-borne sexually transmitted diseases, especially if a male sexual partner does not use a condom, and we know from the microscope and clinical experience that *emperipoletic* lymphocytes seldom migrate through healthy stratified epithelium.

Therefore, until such time that mature, encapsulated HIV-1 retrovirions are demonstrated in blood, colostrum or semen, or actually shedding from any cell contained therein, we should broadcast our message loud and clear that female-choice, as well as male contraceptive barriers, fortified with detergents, such as nonoxynol-9, can prevent the heterosexual spread of AIDS by integrated provirus or non-integrated viral RNA in "Trojan horse" (11) lymphocytes migrating from semen into the female uterus; or from endocervical mucus through the thinned foreskin of an uncircumcised male (12).

In summary, the heterosexual spread of human immunodeficiency virus, Type 1 (HIV-1) infection has become the #1 public health problem among young people in the USA, and throughout the world. Emphasizing the *emperipoletic* nature of small lymphocytes, lymphologists can help many people to

prevent spread of AIDS and other cell-borne sexually transmitted diseases (STD) by urging increased use of female as well as male contraceptive barriers fortified by chemicals stopping the interpersonal migration of infected cells.

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