

Alain Fischer's group in treating SCID-X1 with gene therapy cannot be overlooked. Such trials should proceed with caution. Only by doing so can the true risk of insertional mutagenesis be known.

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Barriers to HIV testing—where next?

HIV infection, if diagnosed early, can be treated to reduce morbidity from opportunistic infections and cancers, and to prolong life. Knowledge of HIV status can also help to reduce transmission. Failure to undergo an HIV test can lead to delayed diagnosis and treatment of life-threatening illness, and to lack of awareness of infectious risk on the part of an infected individual, with serious consequences for individuals and society.

In a recent analysis of the 1998 US National Health Interview Survey,¹ Joseph Inungu found that failure to have had an HIV test was associated with both older (50 years or more) and younger (18 and 19 year olds) age, lower educational level, non-urban residence, and US Midwest location (the lowest prevalence region in the US). Lower education status was also associated with a decreased likelihood of HIV testing in a study in Northern Thailand.² Failure to have an HIV test is often because of a lack of perceived risk on the part of the patient.³ However, in low-prevalence or low-resource settings, testing may not be available at all or, if available, may not have clear benefits, either from a patient's or health worker's viewpoint.⁴ Barriers to HIV testing in different global settings of varying prevalence and economic conditions are complex but can be overcome (panel)—a necessary prerequisite to reversing the AIDS pandemic.⁵

Study of sociological and health-service structures can highlight potentially remediable problems that limit the effectiveness of HIV-testing programmes. Similarly, psychological and anthropological models can suggest relevant and often related obstacles. For example, a woman may reject an HIV test due to her fear of adverse consequences such as rejection or blame from her family.⁶ Her fear may be viewed as a psychological obstacle to

testing. This psychological obstacle is based on the lack of economic or social power of women, introducing a sociological aspect. The reality of the consequences of a positive HIV test is tied to these gender-empowerment issues, and constraints on HIV testing might be driven by powerful social and religious norms.⁷

There are differences in attitudes towards testing depending on the community and medical resources available to the HIV-infected person. In a prosperous country, fear of adverse consequences may be balanced by an awareness of the benefits of HIV-related medical assistance. The converse may be true in a developing country, where the lack of expectation of benefit from an HIV test may reinforce the decision not to seek or accept the test. As benefits increase, rates of HIV testing typically increase; for example, the expansion of HIV test-acceptance rates in pregnant women related to the introduction of antiretroviral therapy to protect the unborn child from HIV infection.⁸ In the USA, the benefits of testing are perceived to be so great that HIV testing has been advocated as a routine test for pregnant women, offered universally.⁹ This approach presumes that prenatal care is available and taken advantage of, that counselling designed to communicate the benefits and risks of testing is available, and that fear, whether that of the patient or of other family members, does not outweigh the desire to protect one's offspring.

There are also many structural and economic issues that impede access to HIV testing. Test kits and testing venues may not be readily available in resource-limited settings or in low-prevalence regions. Prejudice of health-care providers against testing may manifest as poor access to testing or in poor counselling provision.¹⁰ The test may be inconvenient, in that it is not a rapid test with results and confirmation available in less than an hour. People having the test may never return for their results if they must wait weeks for a definitive answer.¹¹ Confidentiality may not be guaranteed and counselling conditions may not provide privacy. Having a test may be socially isolating and provision may not be made for testing partners or other key

Barriers to HIV testing and interventions to increase testing

Barriers to expanded testing

- Fear of adverse consequences
- Lack of expectation of benefit
- No perception of HIV risk
- Cultural norm is not to test or is hostile to testing
- Test is unavailable
- Lack of privacy in counselling
- Lack of guarantees of confidentiality
- Cost
- Inconvenience—eg, same-day testing is not available
- Personal isolation
- Lack of provision for testing couples or social support

Interventions to increase testing

- Offer routine, cheap, convenient test
- Offer test as standard public-health or medical intervention
- Offer test to couples and with social support
- Offer test in package of services, including counselling, clinical care, and prevention education
- Promote test as socially acceptable and seen favourably by families, neighbours, work colleagues, and employers
- Increase awareness of HIV risk and test benefits
- Encourage social norms to shift towards acceptance and support of HIV-infected persons
- Ensure privacy of testing and confidentiality of results

family members whose participation might reduce stigma and fear.^{12,13}

The most worrying barrier is that people might not perceive themselves to be at risk. Sexually active people may recognise personal risk, but not appreciate the risk derived from high-risk behaviour of a partner. Denial of risk is a common coping mechanism. Adolescents, for example, may not feel vulnerable to HIV because of lack of appreciation of the distant consequences of current actions.¹⁴ Innovative public education is essential to cope with such denial.^{15,16}

Testing with effective counselling is vital for HIV control. Pretest counselling itself can have a preventive function, whereas post-test counselling for the infected person can provide a bridge to health-care and other services and reduce personal risk of transmission. Every nation and health establishment would do well to review how voluntary, confidential counselling and testing for HIV can be expanded and promoted.

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Measuring microvascular blood flow in sepsis—a continuing challenge

Sepsis is a major cause of morbidity and mortality in critically ill patients. Although the pathophysiological mechanisms of tissue injury in sepsis depend on activation of several proinflammatory and procoagulant pathways,¹ alterations in microvascular blood flow may, in part, be responsible for the associated multiorgan system failure. Heterogeneous blood flow may result in areas with decreased oxygen delivery or areas with no flow followed by reflow, leading to focal ischaemia and reperfusion injury. However, quantifying microvascular blood flow in patients with sepsis is extremely difficult. A recent report by Daniel De Backer and colleagues² presents a new method for imaging the microcirculation in patients with sepsis and highlights some of the difficulties in making such measurements in critically ill patients.

In the past, two methods have been used for estimating microvascular blood flow in critically ill patients.³ Both techniques have limitations. Nail-fold microscopy visualises only the fingernail capillary bed, a vascular bed that may not reflect blood flow in the systemic microvasculature. Laser doppler fluximetry has been used in other sites, including the gastric mucosa, but this technique averages blood flow in one area and may miss microvascular flow heterogeneity. De Backer and colleagues used orthogonal polarisation spectral imaging, a novel technique that images the microvasculature of a mucosal or solid organ surface.⁴ Polarised light is focused on a small area of tissue. Depolarised reflected light from deep within the tissue is collected by an orthogonal imager, backlighting the more superficial tissue. Since the wavelength is absorbed by haemoglobin, it is possible to visualise red blood cells, and therefore blood vessels, which appear as dark objects against the refracted light background. This non-invasive technique does not seem to be affected by variations in packed-cell volume.

De Backer and colleagues studied the sublingual microvasculature in 50 patients with severe sepsis, measuring vessel density and the proportion of vessels with flow at a single time. 10 healthy volunteers, 16 patients before cardiac surgery, and 5 non-infected intubated patients in intensive care served as controls. Compared with controls, patients with sepsis had lower vessel density and fewer vessels with continuous flow, particularly among smaller vessels (<20 µm). Non-survivors tended to have fewer perfused small vessels although there was substantial overlap between groups. In all 11 patients with sepsis who were tested, topical application of acetylcholine, a vasodilator, increased vessel density and the proportion of vessels with flow.

These findings are a good first step in developing this technique for research and possible clinical use. However, future studies will need to address several important issues. It is not clear in the De Backer study whether the findings are specific for septic shock, or would occur in shock of other causes. Control patients with cardiogenic and hypovolaemic shock need to be studied. The mechanisms behind the alterations in microvascular blood flow also need to be explored. The rapid response to acetylcholine suggests reversal of a vasoconstrictor response, but vasodilation might also overcome intravascular obstruction by leucocytes or thrombus. The effect of fluid balance on the microvascular circulation needs to be better defined especially given recent work demonstrating the benefit of early volume-resuscitation in sepsis.⁵ A more indepth investigation of the relation between flow in the sublingual microcirculation and levels of endogenous and exogenous vasoactive agents would also be of interest. Could the