

INFLUENZA IMMUNISATION IN HIV-INFECTED PERSONS

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Influenza vaccines are widely used throughout the world. Some 80 - 85 million doses are produced annually for distribution in the USA alone¹ where coverage for the major risk group, persons over 65 years of age, was 63% in 1997² (surpassing the 60% vaccine coverage goal for the country's Healthy People 2000 Project). The clinical effectiveness as well as the cost effectiveness of influenza vaccines have been clearly established in a number of studies in many parts of the world.³⁻⁷ Influenza vaccination has also been demonstrated to reduce hospitalisation significantly in elderly high-risk persons.⁸⁻¹⁰ In South Africa, influenza immunisation has similarly been demonstrated to be cost effective¹¹ and utilisation of vaccine in this country has increased markedly over the past few years, reaching over 2 million doses administered in 2000. Annual influenza immunisation is sound preventive medicine generally, and in particular is mandated for persons at risk for complications of influenza.¹²

With regard to influenza immunisation of HIV-infected persons, three issues need to be considered:

(i) are HIV-infected persons at special risk for influenza complications and is annual immunisation specifically advocated for them?;

(ii) is influenza vaccine safe in HIV-infected persons?; and
(iii) is influenza vaccine effective in HIV-infected persons?

IS HIV INFECTION A SPECIAL INDICATION FOR ANNUAL INFLUENZA IMMUNISATION?

Definitive, quantitative epidemiological data on the risk of influenza complications in HIV-infected persons are still not available. However, small-scale studies have shown more severe and prolonged influenza disease in HIV-infected persons.¹³⁻¹⁶ Additional factors which would also need to be taken into account when considering whether HIV infection constitutes a special indication for influenza immunisation include the following:

- (i) uncomplicated influenza illness may involve considerable expense and inconvenience to eliminate a diagnosis of *Pneumocystis* disease in HIV-infected patients presenting with an acute febrile illness;
- (ii) increased influenza virus shedding has been associated with depressed immunity;¹⁷ and
- (iii) the antigenic stimulation of influenza virus infection itself is associated with an increased plasma viral load,¹⁸ one of the concerns raised with influenza vaccine (see below).

The Advisory Committee on Immunisation Practices (ACIP) of the USA has recognised persons infected with HIV as a specific target group for influenza immunisation because of the increased risk of complications.²

IS INFLUENZA VACCINE SAFE IN HIV-INFECTED PERSONS?

Influenza vaccines presently in use are inactive subunit or split-product vaccines and therefore pose no risk of disease directly associated with the vaccine virus, as is the case with the use of live attenuated viral vaccines in immunosuppressed persons. The main concern about administering influenza vaccine to HIV-infected persons has been the observed effect on plasma viral load following administration of influenza and other vaccines. In 1992, a short letter from David Ho in the *Lancet*¹⁹ drew attention to the increase in infectious HIV-1 in plasma and peripheral blood mononuclear cells following influenza infection as well as influenza vaccination. The rise in viraemia was, however, transient and levels returned to baseline by 2 - 3 weeks. Ho further cautioned in the letter that the findings 'should not be used to make clinical decisions about influenza vaccination in HIV-1 infected persons'. A number of publications followed which demonstrated the expected rise in plasma HIV-1 RNA levels following antigenic stimulation and lymphocyte proliferation induced by influenza and other vaccines.²⁰⁻²⁴ It was also noted that influenza vaccine-induced stimulation of HIV replication was more likely to occur in individuals with higher CD4 cell counts, i.e. those individuals who would, in fact, be the most likely to develop an immune response and benefit from the vaccine. However, other subsequent studies have not shown significant increases in viraemia following influenza vaccine administration,²⁵⁻²⁷ or alternatively showed that the rise in viraemia was not only transient and rarely significant but was also not associated with any clinical events.²⁸⁻³⁰ Where transient increases in HIV-1 RNA levels have occurred following vaccination, they have not been followed by any sustained deterioration in CD4 lymphocyte cell counts or progression of disease.³¹

IS INFLUENZA VACCINE EFFECTIVE IN HIV-INFECTED INDIVIDUALS?

Resistance to influenza infection is mediated by humoral immunoglobulin G (IgG) antibodies in plasma and secretory immunoglobulin A (IgA) in respiratory secretions, while recovery from infection, as demonstrated in animal models, is mediated by specific CTL (CD8 cytotoxic lymphocyte) activity. Both immune responses are governed by functionally intact CD4 lymphocytes. It was therefore not surprising that with the progressive decline of CD4 lymphocyte counts there is a corresponding decline in immune response to influenza vaccine. Individuals with CD4 counts less than 200/ml show a poor immune response

to influenza virus infection or influenza vaccination.³² An additional administration of a second dose, however, had no beneficial effect and these non-responding vaccine recipients remained unprotected after a second dose.³³ Asymptomatically infected persons or those with persistent generalised lymphadenopathy were, however, able to mount an appropriate antibody response.³⁴

RECOMMENDATIONS FOR IMMUNISATION OF HIV-INFECTED PERSONS

HIV infection is generally regarded as a specific risk, and it is recommended that affected individuals receive annual influenza immunisation.^{2,35} It is specifically recommended under the following conditions:³⁶

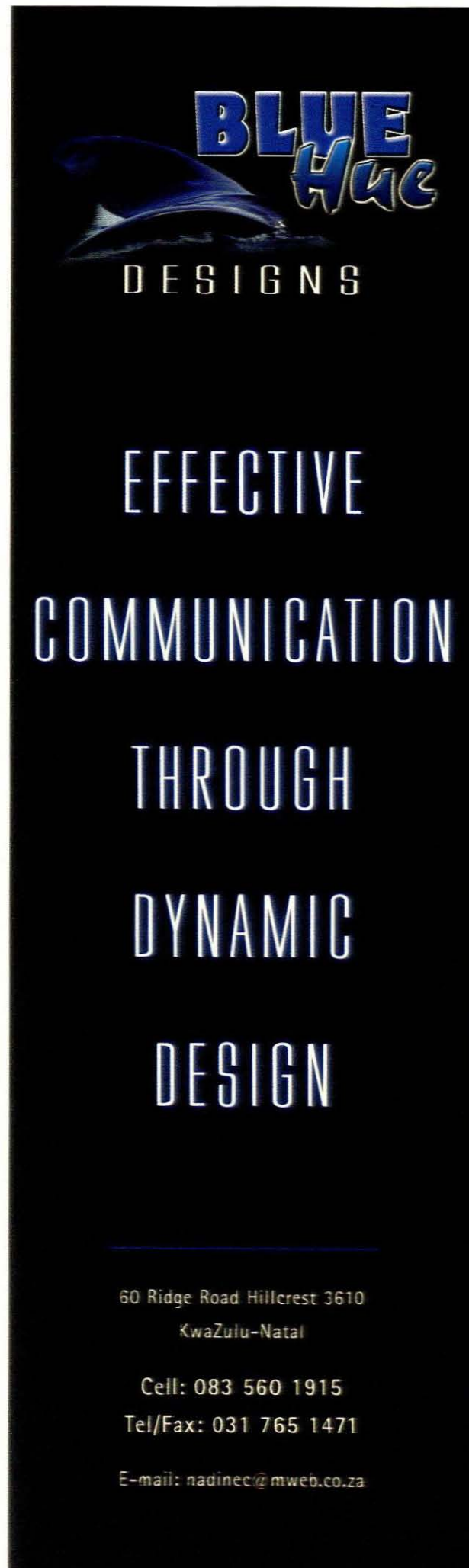
- (i) HIV-infected persons with symptoms and/or CD4 cell counts between 200 and 500/ml;
- (ii) HIV-infected persons with another condition placing them in a higher risk category according to general influenza recommendations;^{2,35} and
- (iii) contacts of HIV-infected patients such as health care personnel and household members.

It is not recommended for HIV-infected persons with CD4 cell counts below 200/ml as they are unlikely to mount an adequate immune response. These individuals should be protected with chemoprophylactic agents such as amantadine (Symmetrel).

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