explore the efficacy of larger doses or additional doses, or both, in those who are seropositive.

In global immunisation programmes the emerging pandemic of HIV infection must lead to a re-examination of the use of vaccines, particularly live ones, in neonates who are likely to be infected with HIV. This problem is most pressing in those countries in which a large proportion of women of childbearing age are seropositive. It affects both the vaccinee, because of failed vaccination or abnormal response to the vaccine, and the whole population, because of the increased burden of microbial infection through the failure of the public immunisation programmes.

In this study we show the impact that coincident HIV infection may have on an otherwise acceptably efficacious vaccine. The efficacy of this and other vaccines in patients infected with HIV needs to be studied urgently.

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References

- 1 Lane HC, Masur H, Edgar L, et al. Abnormalities of B lymphocyte activation and immunoregulation in patients with the acquired immune deficiency syndrome. *N Engl J Med* 1983;309:453-8.
- 2 Mann JM, Francis H, Davachi F, et al. Risk factors for human immunodeficiency virus seropositivity among children 1-24 months old in Kinshasa, Zaire. *Lancet* 1986;ii:654-7.
- 3 Melbye M, Njelesani EK, Bayley A, et al. Evidence for heterosexual transmission and clinical manifestations of human immunodeficiency virus infection and related conditions in Lusaka, Zambia. *Lancet* 1986;ii:1113-5.
- 4 Szmunes W, Stevens CE, Zang EA, Harley EJ, Kellner A. A controlled clinical trial of the efficacy of hepatitis B vaccine (Heptavax B): a final report. *Hepatology* 1981;1:377-85.
- 5 Coutinho RA, Lelie N, Albrecht-Van Lent P, et al. Efficacy of a heat inactivated hepatitis B vaccine in male homosexuals: outcome of a placebo controlled double-blind trial. *Br Med J* 1983;286:1305-8.
- 6 Francis DP, Hadler SC, Thompson SE, et al. The prevention of hepatitis B with vaccine. Reports of the Centers for Disease Control multi-center efficacy trial among homosexual men. *Ann Intern Med* 1982;97:362-6.
- 7 Maupas P, Chiron JP, Barin F, et al. Efficacy of hepatitis B vaccine in prevention of early HBsAg carrier state in children. Controlled trial in an endemic area (Senegal). *Lancet* 1981;ii:289-92.
- 8 Crosnier J, Jungers P, Courouce AM, et al. Randomised placebo-controlled trial of hepatitis B surface antigen vaccine in French haemodialysis units. 1. Medical staff. *Lancet* 1981;ii:455-9.
- 9 Desmyter J, Colaert J, De Groot G, et al. Efficacy of heat-inactivated hepatitis B vaccine in haemodialysis patients and staff. *Lancet* 1983;ii:1323-8.
- 10 Mulley AG, Silverstein MD, Dienstag JL. Indication for use of hepatitis B vaccine, based on cost-effectiveness analysis. *N Engl J Med* 1982;307:644-52.
- 11 Adler MW, Belsey EM, McCutchan JA, Mindel A. Should homosexuals be vaccinated against hepatitis B virus? Cost and benefit assessment. *Br Med J* 1983;286:1621-4.
- 12 Advisory Committee on Immunisation Practices. Recommendations for protection against viral hepatitis. *MMWR* 1985;34:313-34.
- 13 Eichenberg D, Rutherford G, O'Malley P, Bodecker T. Update: acquired immunodeficiency syndrome in the San Francisco cohort study 1978-1985. *MMWR* 1985;35:573-5.
- 13a Carne CA, Weller IVD, Johnson AMJ. Prevalence of antibodies to human immunodeficiency virus, gonorrhoea rates and changed sexual behaviour in homosexual men in London. *Lancet* 1987;ii:656-8.
- 14 McLean AA, Guess HA, Scolnick EM. Suboptimal response to hepatitis B vaccine given by injection into the buttock. *MMWR* 1985;34:105-13.
- 15 Cameron CH, Combridge BS, Howell DR, Barbara JAJ. A sensitive immunoradiometric assay for the detection of hepatitis B surface antigen. *J Virol Methods* 1980;ii:311-23.
- 16 Tedder RS, Cameron CH, Wilson-Croome R, Howell DR, Colgrove A, Barbara JAJ. Contrasting patterns and frequency of antibodies to surface core and e antigens of hepatitis B virus in blood donors and in homosexual patients. *J Med Virol* 1980;6:323-32.
- 17 Hadler SC, Francis DP, Maynard JE, et al. Long-term immunogenicity and efficacy of hepatitis B vaccine in homosexual men. *N Engl J Med* 1986;315:209-14.
- 18 Krugman S, Holley HP Jr, Davidson M, Simberloff MS, Matsaniotis N. Immunogenic effect of inactivated hepatitis B vaccine: comparison of 20 microgram and 40 microgram doses. *J Med Virol* 1981;8:119-21.
- 19 Courouce A-M, Jungers P, Benhamou E, Laplanche A, Crosnier J. Hepatitis B in dialysis patients. *N Engl J Med* 1984;311:1515-6.

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SHORT REPORTS

From persistent generalised lymphadenopathy to AIDS: Who will progress?

About one third of people infected with the human immunodeficiency virus (HIV) have persistent generalised lymphadenopathy and are at risk of developing the acquired immune deficiency syndrome (AIDS). We report on the current rate of progression of persistent generalised lymphadenopathy to AIDS in a cohort of homosexual men in London and the value to the general physician of simple clinical markers for predicting the risk of progression.

Patients, methods, and results

One hundred and five patients who had persistent generalised lymphadenopathy were recruited from this clinic between November 1982 and April 1986 into a study of the clinical course of HIV infection. Five patients were lost to follow up. The remaining 100 patients were followed up for a median period of 24 months (range 9-50). Persistent generalised lymphadenopathy was defined as the presence of lymph nodes greater than 1 cm in diameter in two or more extrainguinal sites for at least three months, other causes for lymphadenopathy having been excluded. The patients were seen at intervals of three months, and all were consistently shown to be positive for HIV antibody by competitive enzyme

linked immunosorbent assay (ELISA). From our previous clinical observations certain features stood out as possible predictors of AIDS—oral candida (found on examination and confirmed on culture) and, if present for more than three months, anaemia (haemoglobin concentration <13 g/l), leucopenia ($<4.0 \times 10^9$ /l), neutropenia ($<2.0 \times 10^9$ /l), lymphopenia ($<1.5 \times 10^9$ /l), thrombocytopenia ($<150 \times 10^9$ /l), and erythrocyte sedimentation rate >15 mm in the first hour. Data were analysed with Fisher's exact test and by calculating the relative risk.

Thirteen patients developed AIDS during a median follow up of 22 months (range 12-32). Five of these developed *Pneumocystis carinii* pneumonia, five Kaposi's sarcoma, one both, one *P. carinii* pneumonia and cryptosporidiosis, and one cryptococcal meningitis. Oral candida were found in nine patients with persistent generalised lymphadenopathy. The following haematological abnormalities had been present for at least three months: anaemia (nine patients), leucopenia (19), neutropenia (18), lymphopenia (24), increased erythrocyte sedimentation rate (15), and thrombocytopenia (four). Oral candida and the first five of these haematological abnormalities were found to be associated with the later development of AIDS (table).

Comment

Of 100 patients with persistent generalised lymphadenopathy followed up for a median of 24 months, 13 developed AIDS. Using a life table technique we calculated that over three years the probability of patients with persistent generalised lymphadenopathy progressing to AIDS was 20.9%. Of the clinical features examined in our study oral candida, lymphopenia, an increased erythrocyte sedimentation rate, and anaemia were found to be the best predictors of the later development of AIDS.

Features associated with risk of progression to AIDS in 100 patients with persistent generalised lymphadenopathy

	Proportion of patients with abnormality who progressed to AIDS	Relative risk	Significance*	Median (range) time before onset of AIDS (months)
Oral candida	7/2	12	$p < 0.0005$	8 (1-24)
Lymphopenia	9/15	7	$p < 0.0005$	19 (2-33)
Erythrocyte sedimentation rate >15 mm in first hour	7/8	7	$p < 0.0005$	23 (10-33)
Haemoglobin <13 g/l	3/4	6	$p = 0.002$	18 (11-33)
Neutrophils $<2.0 \times 10^9$ /l	9/12	4	$p = 0.01$	16.5 (2-21)
White cell count $<4.0 \times 10^9$ /l	9/13	4	$p = 0.02$	16.5 (2-33)
Platelets $<150 \times 10^9$ /l	2/2	4	NS	18.5 (16-21)

*Fisher's exact test.

Similar prospective studies in cohorts of patients with persistent generalised lymphadenopathy in the United States have reported rates of progression from 6% to 19% during median follow up times from 12.9 to 22 months.¹ The rates of progression in cohorts of patients infected with HIV with and without lymphadenopathy ranged from 8% to 34% over three years.² In a cohort of 1835 infected homosexual men followed up for a median of 15 months the annual incidence of AIDS in asymptomatic men compared with that in men with lymphadenopathy was not significantly different.³ Prognostic markers for disease progression include clinical features such as fever and weight loss, oral candida, and leucoplakia, haematological and immunological abnormalities such as anaemia, cytopenias, particularly progressive depletion of T helper lymphocytes, increased serum IgA concentrations, impaired in vitro γ -interferon production, lymphocyte responses to pokeweed mitogen, and perhaps specific cellular responses to HIV.^{3,4} More recently, a decline in the titre or the disappearance of anti-P24 (the antibody to HIV core protein) has been shown to predate the development of the full blown syndrome by up to 27 months.⁵

Many complex tests are not widely available to the general physician, and our study shows that a clinical examination and simple haematological measurements are useful in determining the risk of progression.

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- 1 Weller IVD. The AIDS virus: a new human immune deficiency retrovirus and the natural history of infection. In: Triger DR, ed. *Royal College of Physicians of London. Advanced medicine*. Vol 22. London: Baillière, Tindall, 1986: 141-53.
- 2 Goedert JJ, Biggar RT, Weiss SH, et al. Three year incidence of AIDS in five cohorts of HTLV-III infected risk group members. *Science* 1986;231:992-5.
- 3 Polk BF, Fox R, Brookmeyer R, et al. Predictors of the acquired immunodeficiency syndrome developing in a cohort of seropositive homosexual men. *N Engl J Med* 1987;316:61-6.
- 4 Anonymous. Who will get AIDS? *Lancet* 1986;ii:953-4.
- 5 Weber JN, Clapham PR, Weiss RA, et al. Human immunodeficiency virus infection in two cohorts of homosexual men: neutralising sera and association of anti-gag antibody with prognosis. *Lancet* 1987;ii:119-22.

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A forgotten factor in pelvic inflammatory disease: infection in the male partner

Infection by *Chlamydia trachomatis* has been increasingly implicated in pelvic inflammatory disease in women.^{1,2} While we recognise that pelvic inflammatory disease is often sexually transmitted, we know little about the sexual partners of women with the disease. *C trachomatis* has been isolated in up to half of all men with non-gonococcal urethritis.³ Because some of these patients are asymptomatic they may fail to seek medical treatment and therefore spread the infection.

Methods and results

We studied women who presented at a sexually transmitted disease clinic with features of pelvic inflammatory disease. Their sexual partners in the previous three months were asked to attend for investigation.

All patients were seen by the duty doctor. A full clinical and sexual history was taken. Routine screening for *Neisseria gonorrhoeae*, *Trichomonas vaginalis*, yeasts, and syphilis was performed for all women.⁴ For technical reasons *C trachomatis* culture could not be carried out for all the women. Each patient underwent bimanual pelvic examination. The criteria for diagnosing pelvic inflammatory disease were: (a) lower abdominal pain with or without vaginal discharge, (b) adnexal tenderness with or without adnexal mass, and (c) positive cervical excitation.

Ultrasonography and laparoscopy were performed in three patients because of severe or equivocal physical signs.

Tests on the male contacts were performed only if they had held their urine for over four hours. Non-gonococcal urethritis was diagnosed if a Gram stained urethral smear contained 10 or more polymorphonuclear cells per field (1000 magnification) and microscopy and culture failed to show *N gonorrhoeae*.⁴ Chlamydia cultures were taken from most of the male contacts.

Statistical comparisons were by the χ^2 test (with Yates's correction where indicated).

Fifty eight women were diagnosed as having pelvic inflammatory disease. Of the 45 in whom chlamydia cultures were taken, 16 (36%) gave positive results. One male contact for each of the 58 women was seen. Forty six of these men had non-gonococcal urethritis, of whom 36 were symptom free. The remainder complained of slight urethral discharge or dysuria. *C trachomatis* was isolated from 10 of the 36 cultured, seven of whom were asymptomatic.

Six women admitted to having had a second male partner in the previous three months but these could not be traced. In addition, 11 men admitted to having had another female partner. There appeared to be no relation between concurrent sexually transmitted disease and pelvic infection or non-gonococcal urethritis.

Eleven of the patients with positive chlamydia cultures were taking oral contraceptives in contrast to seven of the 29 with negative chlamydia cultures ($\chi^2=40.07$, $p<0.001$). Only four patients were using an intrauterine contraceptive device.

Comment

The isolation of *C trachomatis* from the cervixes of 36% of women with pelvic inflammatory disease confirmed studies from Scandinavia and the United Kingdom which showed a 30-40% rate in pelvic infection diagnosed at laparoscopy.^{1,2} The present study emphasises the high incidence of non-gonococcal urethritis among the male partners of women with pelvic inflammatory disease, over three quarters of whom were asymptomatic. Kinghorn *et al* studied women with more severe pelvic inflammatory disease than those reported here and showed that 56% of their male contacts had asymptomatic non-gonococcal urethritis.² Our study highlights the need to trace the sexual contacts of all women with pelvic inflammatory disease.

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- 1 Ripa KT, Svenson L, Trehan JD, Westrom L, Mardh PA. Chlamydia trachomatis in patients with laparoscopically verified salpingitis as a result of isolation and antibody determination. *Am J Obstet Gynecol* 1980;138:960-4.
- 2 Kinghorn GR, Duerden BI, Hafiz S. Clinical and microbiological investigation of women with acute salpingitis and their consorts. *Br J Obstet Gynaecol* 1986;93:869-80.
- 3 Holmes K, Handsfield H, Wang SP, et al. Etiology of non-gonococcal urethritis. *N Engl J Med* 1975;292:1199-205.
- 4 Forslin L, Falk V, Danielsson D. Changes in the incidence of acute gonococcal and non-gonococcal salpingitis. *Br J Vener Dis* 1978;54:247-50.
- 5 Bradbeer CS, Thin RNT. Comparison of econazole and isconazole as a single-dose treatment for vaginal candidiasis. *Gynaecological Medicine* 1985;61:396-8.

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Adverse reactions to drugs in children

Most studies of adverse reactions to drugs in children have observed those who received drugs in hospital or at home shortly before admission.^{1,3} As the use of drugs in hospital is considerably different from that outside^{2,4,5} the incidence and nature of adverse reactions might also be expected to vary.

We aimed to discover the incidence and nature of adverse reactions to drugs in a large group of children considered to be representative of the total child population.

Subjects, methods, and results

We surveyed 1590 children over two periods of 13 weeks in the summer and winter of 1984-5. They were pupils or siblings of pupils attending 19 infant care or educational establishments around Birmingham. Parents were asked to record on a weekly questionnaire the drugs being taken by their children, both prescribed and non-prescribed, and whether adverse reactions to the drugs had been seen.