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Patterns of antigenaemia and antibody response in patients infected with human immunodeficiency virus (HIV) according to clinical state

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SUMMARY Five hundred and fifty six subjects, known to be homosexuals or intravenous drug abusers and seropositive for HIV antibody, were selected on the basis of their clinical state—symptom free, lymphadenopathy syndrome (LAS), AIDS related complex (ARC), and AIDS. The presence of antigenaemia and the humoral response to viral polypeptides was investigated. The prevalence of patients positive for p31 antibody was significantly increased in those with AIDS and detectable antigenaemia.

Several observations in subjects infected with human immunodeficiency virus (HIV) have shown that the presence of antigenaemia and decreased antibody titres to major core protein (p24) are correlated with the onset and severity of clinical symptoms.

We studied the presence of antigenaemia and the humoral antibody response to *gag* (p55, p24, p17), *pol* (p66, p51 and p31), and *env* (gp160, gp120, and gp41) products in HIV seropositive subjects grouped on the basis of their clinical condition. Results obtained were analysed to verify whether antibodies to viral proteins, other than core proteins, presented clinically important variations when detectable titres of antigen were found.

Materials and methods

Serum samples obtained from 556 subjects, known to be homosexuals or intravenous drug abusers and selected on the basis of their antibody positivity to HIV, were tested for HIV antigen and antibody. The clinical states of patients was classified as: symtom free (n = 246), lymphoadenopathy syndrome (LAS) (n = 112), AIDS related complex (ARC) (n = 148) and AIDS (n = 50). All serum samples were stored at −20° C without preservatives until use.

All samples were analysed for the presence of HIV antibody by a commercial immunoenzymatic test (HIV Wellcome) performed and interpreted according to the manufacturer's instructions. The analysis of antibody pattern against individual HIV polypeptides was performed by immunoblotting using commercial strips (Du Pont, De Nemours, France) with HIV polypeptides blotted after polyacrylamide gel electrophoresis (PAGE) separation. Each strip was incubated overnight with a 1/100 dilution of serum and the antigen antibody reaction was detected by a rabbit anti-human IgG biotin-avidin system. 4-chloro-1-naphthol was used as substrate. The comparison of blots was made in one session to verify any little variations in the intensity of bands.

Samples were assayed for the presence of HIV core antigen (p24) in a solid phase sandwich-type enzyme immunoassay with anti-HIV p24 fixed on to microtitre plate wells (Du Pont, De Nemours, France).

The presence of HIV p24 was shown by a monospecific biotinylated antibody. The amount of viral antigen was indirectly estimated measuring the amount of bound biotinylated antibody with a streptavidin horseradish-peroxidase conjugate and colour development after the addition of substrate.

All positive reactions obtained by HIV-1 p24 core antigen ELISA were always confirmed by a neutralisation test (HIV-1 p24 core antigen confirmatory test, Du Pont, De Nemours, France).

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Results

PROTEIN RECOGNITION PATTERN OF HIV SEROPOSITIVE PATIENTS

Table 1 shows the percentage of reactivity of individual HIV polypeptides with antibody present in the various groups of human sera. A significant decrease in the percentage of antibody positive subjects, correlated with the increasing severity of clinical condition, was observed against p17, p51, and p55 and to a lesser extent against p31.

Table 2 shows that 146 (26%) of the 556 subjects had detectable amounts of HIV antigen in serum, and

Table 1 *Percentage of antibody reactivity to different HIV polypeptides by immunoblotting in subjects with different clinical conditions*

Polypeptide	Symptom free (n = 246)	LAS (n = 112)	ARC (n = 148)	AIDS (n = 50)
p17	70	64	70	48
p24	87	87	86	76
p31	77	76	81	62
gp41	93	87	91	88
p51	76	64	63	48
p55	84	69	68	64
p66	94	85	86	84
gp120	99	88	95	92
gp160	100	100	99	96

that the percentage of subjects with positive antigenaemia varied only slightly in the first three groups (symptom free, LAS, ARC) with a significant increase ($p < 0.01$) in AIDS patients.

PROTEIN RECOGNITION PATTERN OF HIV SEROPOSITIVE PATIENTS GROUPED ACCORDING TO THE PRESENCE OF A DETECTABLE ANTIGENAEMIA

Table 3 shows the prevalence of antibody against individual HIV polypeptides in relation to the presence or absence of p24 antigen. The decrease in the incidence of subjects' antibody reacting with p17, p24, and p55 in the various groups of subjects selected was more evident in patients with positive antigenaemia. By contrast, the incidence of subjects with serum antibody reacting to p31 was unexpectedly higher in the group with AIDS when antigenaemic subjects were examined alone. No significant differences were observed for other polypeptides.

Discussion

The antibody response to HIV individual envelope proteins occurred in all the sera tested. These data agree with those of other studies[1,2] which show that antibody response to gp120 and gp160 constantly occurs, irrespective of the presence and severity of clinical symptoms.

As already described[3] a decreased percentage of subjects with antibody to core proteins was observed in relation to the severity of clinical symptoms. Various observations have shown that a good percentage of cases with a detectable serum titre of p24 antigen is often associated with a decrease in antibody to core proteins and is related to the presence of more severe illness.[4,5] Our observations are in full agreement with those findings. But our data show that the prevalence of subjects positive for p31 antibody was significantly increased in patients with AIDS and detectable antigenaemia. An increased or persistent antibody response to p31 could, therefore, represent a further marker of a negative clinical outcome of HIV infection.

Table 2 *Percentage of p24 antigen detected in sera from different groups studied*

Clinical state	No of subjects	Percentage of p24 antigen detection
Symptom free	246	21
LAS	112	25
ARC	148	27
AIDS	50	52
Total	556	26

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Table 3 *Percentage of antibody reactivity to HIV polypeptides related to p24 antigen detection in subjects with different clinical conditions*

Polypeptides	Symptom free Ag+ (n = 52)	Ag− (n = 194)	LAS Ag+ (n = 28)	Ag− (n = 84)	ARC Ag+ (n = 40)	Ag− (n = 108)	AIDS Ag+ (n = 26)	Ag− (n = 24)
p17	54	74	79	60	60	74	31	67
p24	77	90	100	83	75	91	69	83
p31	88	74	79	76	85	80	77	50
gp41	88	94	86	88	85	93	85	92
p51	81	74	50	69	60	65	38	58
p55	81	85	86	64	55	74	62	67
p66	96	94	79	88	80	89	77	92
gp120	100	99	86	90	95	96	92	92
gp160	100	100	100	100	100	98	100	92

+ = positive; − = negative; Ag = Antigen.