GROUP- AND TYPE-SPECIFIC ANTIBODIES TO HIV-2 P26 GAG PROTEIN IN SEROPOSITIVE SERUM SAMPLES

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One of the end products of expression of the gag gene of human immunodeficiency virus (HIV), namely protein p24 of type 1 HIV (HIV-1) and p26 of HIV-2, is a dominant viral antigen with a quite conservative set of antigenic determinants. This conservatism manifests itself as ability of the antigen to take part in intertypic cross reactions with antibodies [3], and it follows appropriately from comparison of the primary structures of the gag protein of HIV of the two immunologic types [4]. The presence of common antigenic determinants naturally does not rule out the possible existence of determinants with narrower specificity, both intratypic and strain-specific. Such determinants have been described following analysis of panels of monoclonal antibodies [3, 5].

The contribution of antigenic determinants of the two types to total seroconversion in relation to protein p24/26 gag in natural infection has not been studied. Admittedly from time to time data indicating differences in heterotypic activity of sera toward proteins p24 or p26 gag have appeared. The differences are manifested as inability of antibodies of certain anti-HIV positive sera to take part in interaction, recordable by means of immune blotting, with heterotypic p24/p26 gag antigens. However, for reasons that will be clear, by this approach, homotopic activity is always higher than heterotypic, so that the differences in heterotypic activity mentioned above can be most easily explained by different initial antibody titers in the sera.

In the present investigation a technique of radioimmunoprecipitation assay (RIPA) was used for analysis; the efficacy of antibody detection in a heterotypic system in this case was significantly higher than in a homotypic system. During analysis of a panel of sera to HIV-2 we were convinced that in one case seroconversion is limited by type-specific antibodies.

EXPERIMENTAL METHOD

HIV-1 infected cells and cells of lymphoid strain CEM, infected with HIV-2, strain CBL-20 (obtained from Dr R. Weiss) were incubated with ^{14}C-amino acids and used for RIPA, as described previously [1, 2].

Sera containing antibodies to HIV-2 were used: six specimens from the official WHO panel (obtained from the National Institute for Biological Standards and Control, London) and one specimen (33875) was obtained from Dr R. Argirova (Sofia). Sera were obtained from HIV-2 infected inhabitants of various countries in West Africa. Seronegative sera and serum containing anti-HIV-1 were used as the control.

EXPERIMENTAL RESULTS

The experiments consisted of setting up RIPA with sera containing anti HIV-2, in a homo- and heterotypic version, i.e., with extract containing ^{14}C-proteins of HIV-2 and HIV-1 respectively. The results are given in Fig. 1. Initially the most useful course was to examine the results of homotypic RIPA. It will be clear that the sera precipitated viral glycoproteins with high molecular weight, namely gp170 and gp160 for HIV-2 and HIV-1 respectively, the so-called gag precursor, p57 and p55, and also

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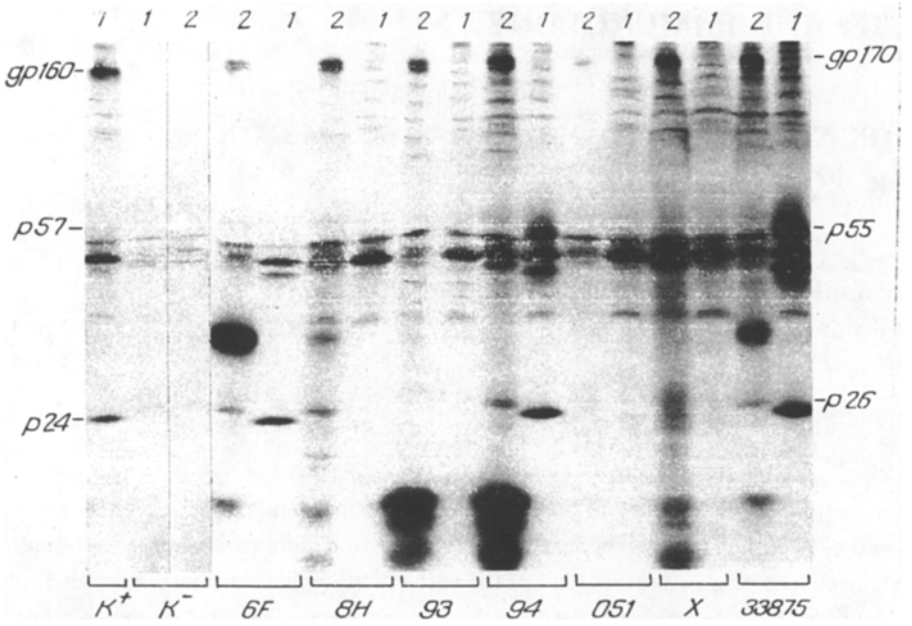

Fig. 1. Analysis of homotypic and heterotypic activity of serum to HIV-2 by RIPA. Cell extracts containing HIV-1 (lanes 1) and HIV-2 (lanes 2) ^{14}C-proteins were used for RIPA with sera to HIV-2 (indicated below each pair of lanes). The letter "K" denotes control: K^-) extracts of HIV-1 and HIV-2, precipitation with seronegative serum, K^+) extract of HIV-1, precipitation with seropositive serum.

gag proteins p26 and p29. Sera, especially in the reaction with HIV-2 antigen, also precipitated other proteins, the nature of which will not be examined here.

Only four specimens from the seven sera to HIV-2 precipitated protein p26 gag in the homologous RIPA, and all the sera, moreover, were active against protein gp170, i.e., they truly contained antibodies to HIV-2. Three of these specimens (6F, 94, and 33875) also precipitated p24 gag HIV-1 in the heterologous reaction.

In one case (8H) only the homologous antigen, p26 gag, was found in the immunoprecipitates, and only the heterologous antigen in the other (051). Sera 93 and X had no anti-gag activity in either homotypic or heterotypic versions of RIPA. Thus the distinctive features of the system of analysis used are such that activity of group-specific antibodies in the heterologous reaction were discovered with not less efficiency, but with even greater efficiency as regards the level of irradiation of the film than the combined anti-p26 gag activity in the homologous reaction. This state of affairs facilitates interpretation of the data obtained during analysis of the 8H serum: by contrast with other specimens the ratio between group- and type-specific antibodies in it was sharply displaced toward the latter. In fact, with marked combined anti-p26 activity discovered in the homologous RIPA, activity of antibodies in the heterologous reaction under conditions extremely favorable for their detection, could not be found.

It will be clear that the explanation of the phenomenon we have found must be based on one of two principal alternatives: the more rapid release of group-specific antibodies in the individual who was the source of the 8H serum, or reduced efficiency of antibody formation. Staphylococcus A was used as the carrier for detecting immunoprecipitates in the present investigation, and for that reason only antibodies of the IgG class were analyzed. It is quite difficult to imagine a situation in which antibodies which differ only functionally, but are analogous in structure, could have a significantly different life span in vivo. However, the rate of release could be controlled by means of an intermediary. Such an intermediary could be a certain "third" virus (i.e., neither HIV-1 nor HIV-2), and with marked crossed antigenic properties with HIV-2 with respect to gag gene proteins. Effective replication of this virus in vivo could lead to exhaustion of group-specific antibodies to p26 gag of HIV-2 due to their binding and release with immune complexes.

As regards the idea of the unequal efficiency of formation of group- and type-specific antibodies to p26 gag, this may be a question of differences in regulation of the immune response in the patient who was the source of the 8H serum. In this case it would be fortuitous to consider only matching of the antigenic determinants as subjects of regulation of the immune response to their separation into group- and type-specific.

The practical importance of the phenomenon described above is that it demonstrates the fundamental impossibility in this and similar cases of establishing a correct serologic diagnosis of HIV infection if the immunologic types of the virus (or its analog) used in the test system are not identical with those of the virus that is the source of infection.

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EXPERIMENTAL STUDY OF THE ROLE OF THE LOCAL INFECTIOUS FOCUS IN DEVELOPMENT OF *Pseudomonas aeruginosa* SEPTICEMIA

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Ideas on the link between the local infectious process and the development of septicemia are still debated. These views have varied from accepting that pathological changes in the body at a certain stage of a disease are independent of the state of the primary focus [1, 3] to concluding that the view that the local and generalized processes are separate [4, 7] and that the disease is reversible after removal of the primary focus [6] are unjustified.

The solution of problems of the etiology and pathogenesis of septicemia extends far beyond the bounds of theoretical polemic, for it plays an exceptionally important role in the determination of the therapeutic tactics in relation to patients with infected wounds. The aim of this investigation was to study how the development of septicemia and the appearance of metastatic pyemic foci in an experimental model depend on the state of the primary septic focus and the time of its removal.

EXPERIMENTAL METHOD

Experiments were carried out on 156 noninbred male albino rats weighing 180-200 g. A local infectious process was produced by a single intramuscular injection of 0.3 ml of a suspension of a 24-h culture of microorganisms in a 10% solution of $CaCl_2$ containing $8 \cdot 10^9$ bacterial cells in 1 ml. The strain of *Pseudomonas aeruginosa* No. 453 which was used was obtained from the Culture Museum of the L. A. Tarasevich Research Institute of Standardization and Control of Medical and Biological Preparations. The use of this strain in a method of obtaining an experimental model of septicemia developed previously, leads to

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