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Zidovudine (AZT) Resistance in a Cohort of Patients at the London Hospital

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We are continuing to monitor viruses from a cohort of 170 patients at the London Hospital for sensitivity to AZT on a biological, clinical and molecular basis. Primary isolation of AZT-sensitive HIV (HIV^S) and AZT-resistant HIV (HIV^r) is carried out by cocultivation of patients' peripheral blood mononuclear cells (PBMC's) with uninfected PHA stimulated PBMC's in the presence and absence of AZT and by monitoring p24 antigen in the culture supernatant. Further characterisation of HIV^S and HIV^r is by growth and passage in PBMC's and other cell types; AZT-sensitivity assays and evaluation of cross-resistance with other antiretrovirals. The DNA base sequence of part of the gene encoding for the reverse transcriptase (RT) enzyme is elucidated. In patients who are documented as never having received AZT, at a screening level of 1μM AZT we have isolated HIV from 13% of samples. At 5μM AZT we have no positive isolations from this group. In the absence of AZT we have isolates from 32% of samples. From patients who have received AZT at a screening level of 1μM AZT we have HIV isolates from 43% of persons. At 5μM AZT we have been successful with 27% of the samples. In the absence of AZT we have isolated HIV from 57% of samples. Our reference strain of HIV^r has proved resistant to all concentrations of AZT tested up to 125μM and has shown some cross-resistance to DDI. Other HIV^r's have shown varying degrees of AZT-resistance and no cross-resistance to date. Molecular analysis has revealed mutations from the wild-type RT. Some of these mutations are the same as those already described in the literature and these will be presented. We have been able to propagate few strains of HIV^S or HIV^r in continuous cell lines. In some patients AZT-resistance correlates with a rise in p24 antigenaemia and a reduction in the CD4 count and we have selected eight patients for a more detailed study to be presented here.

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A STUDY OF THE DEGREE OF THE INFLUENZA VIRUS A SENSITIVITY TO RIMANTADINE. V.Kalnina and M.Indulen. Institute of Microbiology, Latvian Academy of Sciences, Riga, Latvia, USSR.

We demonstrated earlier in experiments upon consequent passages in the presence of rimantadine or amantadine of influenza A virus strains sensitive to them (HINI, H2N2, H3N2) there quickly appear virus varieties, resistent to the drugs (V.Kalnina, 1982). Expedient seems a regular control of the sensitivity to antiinfluenza drugs of the recently isolated influenza A virus taken in places both, where influenza is prophylaxed and treated with rimantadine and amantadine and where influenza chemotherapy is not used. Tests on influenza virus sensitivity to the drugs were undertaken parallely in MDCK and CAM cultures. The sensitivity cryterion was the index ED_{50} - drugs concentration inhibiting virus plaque formation by 50% (in MDCK) or the yield of the infectious virus (in CAM) upon the infection 100ID per sample. We demonstrated the degree of the rimantadine-sensitivity of influenza virus epidemic strains isolated in different years (from 1979 to 1990) in various places (Riga, Moscow, Leningrad, Kiev, London, Berlin) to vary. Along with highly sensitive viruses (87,3%) there were revealed strains with a decreased sensitivity (9,7%) and a number of resistent isolates (3,0%). However, no tendency was observed of arise in the per cent of influenza A virus strains resistent to rimantadine in those cities where a wide rimantadine-prophylaxis of influenza is carried out.