

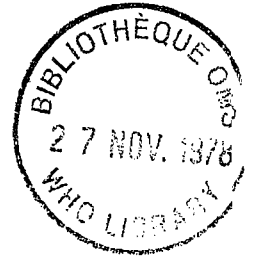


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LABORATORY ASPECTS OF THE MONKEYPOX VIRUS/WHITEPOX VIRUS PROBLEM

by

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Human monkeypox, a disease now being reported only from Zaire, is a rare zoonosis of limited public health importance. Although the human disease is indistinguishable from smallpox, the causative virus differs in many ways from variola virus. The possible existence of an animal reservoir of variola virus remains a potential threat because of the recovery of 6 strains of "whitepox" virus (which is indistinguishable from variola virus but of unknown human pathogenicity) from 5 species of wild animal.

A meeting was called on 9-10 November 1978 to discuss ways of evaluating recent experimental evidence from Dr Marennikova's laboratory that whitepox virus was derived by direct mutation from monkeypox virus. If correct, this would explain the existence of whitepox virus, but would change the significance of monkeypox virus as a potential threat to smallpox eradication.

It has long been known that all orthopoxviruses that ordinarily produce haemorrhagic pocks on the CAM also produce a small proportion of "white" pocks that breed true. Over the past few years these have been described for monkeypox virus, and four strains isolated in England and Holland were found by various tests (Tables 1 and 2) to be very like the parental monkeypox virus and quite unlike variola virus. Early this year, Dr Marennikova and her colleagues reported that they had obtained a total of 9 stable clones of white pock variants, from two different strains of monkeypox virus, by tests on the CAM and in hamsters. All 9 resembled whitepox virus (and thus variola) by all the biological and serological tests used (see Table 2).

To resolve these contradictory findings, the meeting agreed to exchange materials and carry out further tests, as well as attempt to repeat Dr Marennikova's experiments in their centres. Although the planned experiments may take several months to complete they should provide an unequivocal answer.

To explain the technical aspects of WP/78.48B, it may be useful to list the "hierarchy" of tests used by viral geneticists to compare closely related viruses and illustrate what tests have been and will be applied to the white variants of monkeypox (Table 1).

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TABLE 1

The Hierarchy of Comparative Tests

1. Comparison of genomes
 - a) sequence analysis of DNA (impracticable for poxviruses)
 - *b) restriction enzyme analysis
 2. *Comparison of polypeptides (the primary gene products)
 3. Comparison of particular gene products
 - *a) viral enzymes
 - *b) viral antigens: monkeypox virus has "mo" antigen
variola and whitepox have "va" antigen
vaccinia virus has "va" and "vc" antigens.
 4. *Biological properties:

Pock character, growth in particular cell cultures, pathogenicity for mouse, rabbit, chick embryo, ceiling temperature, etc.

*All these tests have been applied to variola, whitepox, and wild-type (haemorrhagic pock) monkeypox virus and show that variola and whitepox viruses are identical and quite different from monkeypox virus.
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TABLE 2

Results and Proposed Tests with White Variants of Monkeypox Virus

1. *Restriction enzyme analysis of genomes

Dumbell: one white pock variant like monkeypox and unlike variola.
2. *Polypeptide analyses

Bedson/Harper: one white pock variant like monkeypox and unlike variola.
3. Enzyme comparison

Bedson/Harper: same (No.2) white pock variant like monkeypox and unlike variola.'
4. "Specific" antigens

Gispen/Hekker: two white pock variants have "mo" antigen and not "va".
Marennikova: nine white pock clones have "va" and not "mo".
5. Biological characters

Gispen/Hekker: two white pock variants like monkeypox in PEK cells.
Marennikova: nine white pock clones like whitepox/variola and unlike monkeypox.

*Tests to be applied to Dr Marennikova's white pock clones.