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Serologic Response to BK Virus following Human Infection with SV40 (39343)

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Evidence was presented in a previous paper (1) suggesting that infection in man with BK virus, a recently discovered human papovavirus, could induce low levels of antibody to SV40. An opportunity to examine the converse question, as to whether infection in man with SV40 could induce antibody to BK virus, was made possible by the retrieval and testing of sera from a unique earlier study in volunteers infected with respiratory syncytial virus (RSV) which was later found to contain live SV40 (2).

Materials and methods. Paired sera were available from 34 of the original group of healthy adult males who had been given a nasal instillation of 10,000 $TCID_{50}$ of SV40, in addition to RSV with or without antiserum. In this earlier study, antibody to SV40 in pre- and postinfection sera, starting at a 1:5 dilution, had been determined in neutralization tests using 250 $TCID_{50}$ of SV40 in tubes of grivet kidney cells (2). Most of the postinfection sera had been obtained between 2 and 4 weeks after infection, but a few were collected as early as 10 days, or as late as 90 days, after infection. Sera were stored continuously at −20° since completion of this study in 1960. In the present study, aliquots of these sera were extracted with acetone to give an initial dilution of 1:20, and antibody to BK virus was determined in a hemagglutination-inhibition (HI) microtiter test, which is more sensitive than the neutralization test, and can detect antibody to BK virus in sera stored at −20° for at least 15 yr (1).

Results. As shown in Table I, 18 of the 34 subjects who had received SV40 became seropositive to SV40, with neutralizing antibody titers ranging from 1:5 to 1:80. None of these subjects showed any rise in HI antibody to BK virus, whether or not they had demonstrated pre-existing BK antibody. In one of them, who presumably had experienced a natural infection with BK virus shortly before being infected with SV40, the level of BK antibody fell from 1:2560 to 1:40 during a 3-month period following administration of SV40.

Discussion. A small but definite degree of antigenic sharing between SV40 and BK virus has been demonstrated in serological studies using hyperimmune animal sera. Employing the immune-electron microscopy test, a weak reaction has been observed between BK virus and SV40 antisera, and between SV40 and BK virus antisera (3, 4). A similarly weak reciprocal cross reaction between SV40 and BK virus has been shown to occur in fluorescent antibody tests (5). Antisera to BK virus also show low neutralizing activity against SV40 in plaque-reduction tests, and in tissue cul-

TABLE I. ANTIBODY RESPONSES TO SV40 AND BK VIRUS IN 18 HUMAN VOLUNTEERS INFECTED WITH SV40.

Subject	BK virus HI antibody titer		SV40 Neutralizing antibody titer[a]	
	Preinfection	Postinfection	Preinfection	Postinfection
No pre-existing BK antibody				
1	<20	<20	<5	5
2	<20	<20	<5	5
3	<20	<20	<5	5
4	<20	<20	<5	10
5	20	<20	<5	10
6	<20	<20	<5	20
7	<20	<20	<5	>20
Pre-existing BK antibody				
8	40	40	<5	5
9	40	40	<5	5
10	80	80	<5	5
11	40	40	<5	10
12	40	40	<5	10
13	80	40	<5	10
14	40	40	<5	>20
15	40	40	<5	>20
16	40	40	<5	>20
17	80	80	<5	80
18	2560	40	<5	80

[a] Data from original study (2).

ture, BK virus induces T-antigen(s) immunologically similar to or identical with the SV40 T-antigen(s) (5). No cross reactions between the two viruses have been observed by HI (5), CF (3, 5), immunodiffusion (6), or immunoelectrophoresis (6).

These data raise the question of virus responsibility for the antibody patterns seen in man. Vaccine and monkey sources of SV40 infection are known to account for most of the SV40 antibody found in humans (7), and circumstantial evidence suggests that BK virus infection accounts for virtually all the rest (1). Evidence presented in the present study indicates that, in contrast, proven human infection with SV40, even in individuals with substantial homologous antibody responses, does not induce cross-reactive HI antibody to BK virus.

Summary. A small group of human volunteers given live SV40 virus, and who seroconverted to SV40, did not develop any heterologous antibody response to BK virus, even when BK antibody was demonstrated in preinfection sera. SV40 infection does not appear to contribute significantly to the patterns of BK antibody seen in human populations.

1. Brown, P., Tsai, T., and Gajdusek, D. C., Amer. J. Epidemiol. **102,** 331 (1975).
2. Morris, J. A., Johnson, K. M., Aulisio, C. G., Chanock, R. M., and Knight, V., Proc. Soc. Exp. Biol. Med. **108,** 56 (1961).
3. Gardner, S. D., Field, A. M., Coleman, D. V., and Hulme, B., Lancet **1,** 1253 (1971).
4. Penney, J. B., Jr., and Narayan, O., Inf. Immun. **8,** 299 (1973).
5. Takemoto, K. K., and Mullarkey, M. F., J. Virol. **12,** 625 (1973).
6. Mullarkey, M. F., Hruska, J. F., and Takemoto, K. K., J. Virol. **13,** 1014 (1974).
7. Shah, K., Amer. J. Epidemiol. **95,** 199 (1972).

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