Prevalence in England of Antibody to Human Polyomavirus (B.K.)

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Summary

Over 500 human sera were tested by complement fixation and haemagglutination inhibition tests for antibody to the human polyomavirus (B.K.). Both tests showed that antibody to this virus was very common in the population and began to be acquired after the age of 1 year. No clinical illness has so far been associated with the development of this antibody in a series of paired sera from children.

Introduction

Gardner *et al.* (1971) described the isolation of a polyoma-like virus (B.K.) from the urine of a Sudanese patient who developed ureteric obstruction four months after a renal transplant operation. The virus was recovered from his urine on five separate occasions over a period of 16 days, and a noticeable increase in antibody to this virus was found in serial sera obtained from him. Both the patient and his donor brother were found to have antibody at the time of the transplant.

B.K. virus belongs to a group of animal viruses which have an oncogenic potential. As it was isolated from man it was clearly of importance to determine how common it was in the population and whether it was associated with any particular clinical condition.

A serological survey was therefore begun to assess the prevalence in England of antibody to this apparently new virus by the techniques of complement fixation and haemagglutination inhibition.

The results of these investigations are presented in this report.

Materials and Methods

Serum Samples.—Over 500 sera were obtained from various sources as follows: (*a*) single sera from infants, children, and adults aged between 26 and 50 years submitted for cytomegalovirus studies or antistreptolysin O estimations; (*b*) sera from healthy university students; (*c*) sera from healthy adult volunteers over the age of 50 years; (*d*) sera from healthy children attending primary schools in North-west England, given by Dr. D. Reid; and (*e*) paired sera from children suffering from a variety of clinical illnesses, kindly supplied by Dr. M. H. Hambling.

Antibody Tests.—Details of the preparation of antigens and techniques used for the complement fixation (C.F.) and haemagglutination inhibition (H.I.) tests have been described (Gardner *et al.*, 1971). The H.I. test was slightly modified and a micromethod was used with unit volumes of 0·025 ml. Serial twofold dilutions of serum from 1/20 to 1/20,480 were made in disposable plastic plates using Microtiter loops supplied by Cooke Instruments Ltd., and 8-16 haemagglutinating units were added to each serum dilution. Titres of 40 or more were regarded as specific. In the C.F. test sera were screened initially at a dilution of 1/8 and those showing fixation at this level were then titrated. Sera from some age groups which were C.F.-negative at this dilution were retested at lower dilutions when H.I. antibody was shown to be present.

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Results

The distribution of C.F. and H.I. antibody to B.K. virus at various ages is shown in Tables I and II.

TABLE I—*Complement-fixing Antibody to B.K. Virus in Human Sera*

Age Group	No. of Sera Tested	No. of Sera with Antibody	Percentage with Antibody	Range of Titres
0–3 months	40	14	35	8–256
4–11 „	57	3	5	2–16
1–5 years	50	18	36	4–64
6–10 „	68	48	71	4–64
11–17 „	70	45	64	⩾4
18–25 „	130	92	71	8–64
26–50 „	44	30	67	2–16
>50 „	49	26	53	2–32
Total	508	276	54	

TABLE II—*Haemagglutination-inhibiting Antibody to B.K. Virus in Human Sera*

Age Group	No. of Sera Tested	No. of Sera with Antibody	Percentage with Antibody	Range of Titres	Percentage Sera with Titres 2,560 or Greater
0–3 months	36	24	67	40–5,120	25
4–11 „	54	2	4	40–160	0
1–5 years	46	17	37	40–5,120	11
Primary schoolchildren (4–6 years)	48	35	73	40–5,120	31
6–10 years	52	43	83	160–⩾20,480	35
11–17 „	40	33	83	40–⩾20,480	36
18–25 „	34	27	79	40–2,560	4
26–50 „	46	33	72	40–10,240	20
>50 „	53	40	75	40–⩾20,480	8
Total	409	254	62		

The results with both tests showed that a substantial proportion of people in England have antibody to this virus. This developed rapidly after the age of 1 year, and in this series by the age of 10 years 71% of children had C.F. antibody and 83% had H.I. antibody.

The proportion of persons with C.F. antibody began to decline after the age of 50 years, and after the age of 25 years the titres were, on the whole, lower. By the age of 50 years only 33% of people had titres of 8 or more. When titres of 2 or more were considered, this percentage rose to 53. Both values are shown in table I.

The H.I. test is a more sensitive method than the C.F. for detecting antibody. The percentage of persons with H.I. antibody in the older age groups was only slightly lower than that seen in children and young adults.

Generally there was good correlation between the results of the two tests. Sera with the highest C.F. titres had correspondingly high H.I. titres. It was possible to find H.I. antibody in all C.F.-positive sera with the exception of two C.F.-positive infants. One mentally retarded infant of 9 months and a second infant aged 10 months with jaundice had C.F. titres of 16 and 8 respectively but neither had developed H.I. antibody. Another mentally retarded infant aged 4 months had a C.F. titre of 1/2 and an H.I. titre of 1/40. In this case the low levels of antibody may have been passively acquired from the mother.

Since many of the sera tested were from ill children these results might not give a true picture of the prevalence of antibody. Sera from a group of healthy primary schoolchildren were therefore examined and, as shown in table II, the incidence of antibody in this group was of a similar order.

The highest incidence of antibody to B.K. virus occurred between the ages of 6 and 17 years. It is also in this age range that the proportion of sera with high H.I. titres of 2,560 or greater were found (table II). The highest C.F. titres were observed in the age group 1-10 years. These findings suggest that the virus is actively transmitted throughout the period of childhood.

In an attempt to associate infection with some clinical condition a small number of paired sera were examined. These were obtained from children suffering from a wide range of undiagnosed illnesses of a possible viral aetiology. No seroconversions or fourfold increase in titres were found (table III), and the distribution of antibody was similar to that in other groups.

TABLE III—*Haemagglutination-inhibition Antibody to B.K. Virus in Paired Sera from Children*

Age	No. of Paired Sera Examined	No. of Paired Sera with Antibody	Range of Titres	No. of Paired Sera Showing a Seroconversion or Fourfold Rise in Titre
6–11 months	3	0	—	—
1–5 years ..	18	6	640–20,480	0
6–9 „ ..	10	9	80–10,240	0

Discussion

It has been known for some time that polyoma-like viruses may exist in man. ZuRhein and Chou (1965) described particles, morphologically identical with polyomaviruses, which they observed in brain cells in a rare neurological disease—progressive multifocal leucoencephalopathy.

All attempts to culture this virus were unsuccessful until, by using human fetal glial cells, Padgett *et al.* (1971) reported the isolation of a virus (J.C.) from a brain extract of a patient with progressive multifocal leucoencephalopathy. This virus appeared to be unrelated to the mouse polyomavirus and simian virus 40 (SV_{40}). The frequency of antibody to this J.C. virus in the general population has not been described.

Further virus isolations from two additional cases of progressive multifocal leucoencephalopathy have been reported (Weiner *et al.*, 1972). In these cases the viruses isolated were thought to be identical with SV_{40}.

Antibody to SV_{40} virus has been found in sera from persons who received contaminated poliovaccine or who had contact with monkeys, both known sources of this virus. It has also been found in persons not in these categories (Shah, 1972). However, the number of persons with antibody has been found to be small and the titres low. This suggested that if another source of SV_{40} exists or if there is an antigenically identical human virus, infection is not common. Shah *et al.* (1971) suggested the possibility that the antibody detected in these persons might be the result of a cross-reaction with another member of the polyoma-SV_{40} group of viruses.

With the report of the isolation of the polyoma-like virus (B.K.) from the urine of an immunosuppressed patient it was evident that infection can occur in man without involving the central nervous system. In this patient virus particles were found by electron microscopy in infected ureteric cells as well as in the urine (Gardner *et al.*, 1971). The presence of antibody before the renal transplant in both patient and donor suggested that the virus could be common in man and with immunosuppressive therapy could become activated.

The serological results presented in this paper indicate that infection with B.K. virus is indeed widespread. However, no clinical illness has so far been associated with the infection nor is it known yet how the virus is transmitted.

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Oxygen Transport in Acute Pulmonary Oedema and in Acute Exacerbations of Chronic Bronchitis

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Summary

When breathing air, the average arterial oxygen tension in eight patients with acute pulmonary oedema was significantly higher than in eight other patients suffering from an acute exacerbation of chronic bronchitis, but the mixed venous oxygen tension was very similar in both groups. This largely arose from the smaller arteriovenous difference of oxygen content in the bronchitic cases, presumably due to their higher cardiac output, associated with raised arterial CO_2 tensions. Oxygen therapy (60-90% for pulmonary oedema, 30% for the bronchitics) raised the mixed venous oxygen tensions to a similar level in both groups. We suggest that the major need for oxygen therapy lies in patients who maintain their oxygen consumption but show a reduction in mixed venous tension when breathing air. Although partial correction of arterial hypoxaemia is adequate in chronic bronchitis—in which the cardiac output is maintained—high concentrations of oxygen are necessary in pulmonary oedema, in which the cardiac output is low.

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Introduction

Most agree that hypoxia should be corrected in both acute and pulmonary oedema and in acute exacerbations of chronic bron-