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Measles in monkeys: an epidemiological study

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SUMMARY

This study describes aspects of measles in non-human primates. Monkeys infected before importation are shown to produce non-immune offspring in captivity in England. The high antibody titres found in most recently imported monkeys decline slowly during captivity in England. While measles is often fatal to monkeys, we have described an outbreak in which a number of symptomless infections occurred. Histological examination of fatal cases produced evidence of infection in the wall of the urinary bladder in one monkey. The close similarity between measles in humans and monkeys has been confirmed. It is considered that the study of infection among the latter may have significance for the former.

INTRODUCTION

Increasing numbers of apes and monkeys are now bred in captivity for conservation purposes or for research. Monkeys in the wild are free from measles, only contracting infection when they come into contact with humans (Meyer *et al.* 1962). The severity of the disease varies. Some outbreaks result in the death of all the animals, whilst others are non-fatal.

Human maternal measles antibody crosses the placenta, but is destroyed during the first weeks of infant life. If the same is true among other primates an increasing population of captive-born apes and monkeys is at risk of infection from human sources, with potentially serious consequences.

In view of this threat and because human and simian measles are closely similar in their pathology (Scott & Keymer, 1975), we investigated the titres of measles antibody among groups of primates in various situations.

MATERIALS AND METHODS

Sera from five groups of monkeys were examined for measles haemagglutination inhibition (HAI) antibody using Tween-ether extracted antigen (Burroughs Wellcome) and freshly collected rhesus monkey red-cells in Alsever's solution.

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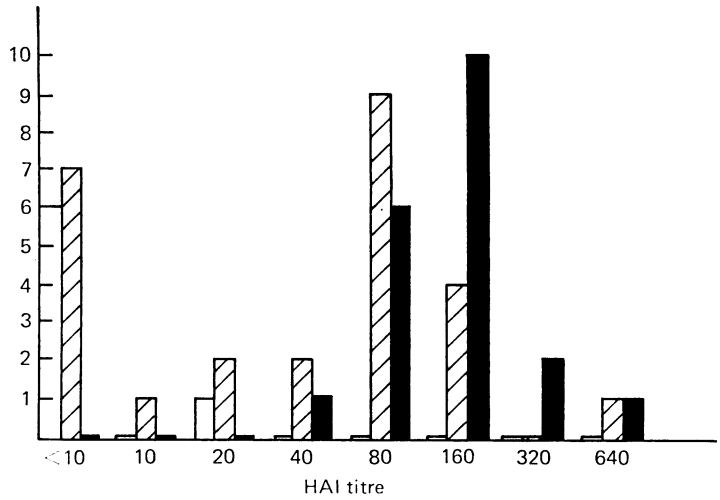

Fig. 1. HAI titres in groups 1–3. □, Group 1. Animals, 9–12 months old, born in England, ▨, Groups 1 and 2. Animals, adult, imported more than 2 years earlier. ■, Group 3. Animals, adult, recently imported.

All sera were absorbed overnight at 4 °C with 50 % monkey red-cells before testing. The tests were done by a microtitre method, using 25 μl volumes of reagents.

Group 1 comprised six wild-born, female rhesus monkeys (*Macaca mulatta*) held in captivity for over 2 years in an English safari park, together with seven of their offspring born in captivity and aged between 9 and 12 months. It was not possible to relate individual offspring to particular mothers.

Group 2 consisted of 20 other wild-born rhesus monkeys of mixed ages and both sexes, living in the same colony as group 1.

Group 3 consisted of 20 recently imported rhesus monkeys which were bled within 1 month of their arrival in England.

Group 4 comprised two chimpanzees (*Pan troglodytes*), four talapoins (*Cercopithecus talapoin*) and four spider monkeys (*Ateles* spp.) housed at the Zoological Society of London. Both the chimpanzees and two of the talapoins were born in this country, while the spider monkeys and the remaining two talapoins were wild-born. Blood samples were obtained during brief admissions to the animal hospital. Complete clinical records were available.

Group 5 consisted of 72 rhesus monkeys imported from India. Within a few days of arrival a large proportion of the group developed clinical measles. Ten days after importation, at the beginning of the measles outbreak, blood was taken for serological examination from 61 animals. A second sample was taken from 24 of these animals 14 days later. Eight animals were then selected to be bled at monthly intervals for a further 7 months. Individual clinical records of all illnesses were kept for the whole period of study. Any animal which died was examined by autopsy and a selection of tissues was removed for histology. The sera from the last bleeding were examined for complement fixing (CF) antibody against Influenza A virus and Cytomegalovirus (CMV) as well as measles HAI antibody.

Table 1. *Measles HAI titres of group 4 animals (London Zoo)*

Species	Captive-born (c) or imported (i)	Measles HAI titre
Chimpanzee	c	64
Chimpanzee	c	32
Talapoin	i	32
Talapoin	i	< 4
Talapoin	c	< 4
Talapoin	c	< 4
Spider monkey	i	64
Spider monkey	i	< 4
Spider monkey	i	< 4
Spider monkey	i	64

RESULTS

Group 1 (animals 9–12 months old, born in England)

Among the offspring born in captivity six had titres of less than 10, and the seventh a titre of 20 (Fig. 1).

Groups 1 *and* 2 (adult animals imported more than 2 years earlier)

Of these 26 animals, seven had titres below 10, one of 10, two of 20, two of 40, nine of 80 and five had titres of 160 or higher (Fig. 1).

Group 3 (adult animals, recently imported)

Antibody titres among 20 recently imported adults ranged from 40 to 640, 13 having titres above 80 and only one below 80 (Fig. 1).

Group 4

Of the imported animals in this group one talapoin and two spider monkeys had titres of less than 4 (Table 1). The second imported talapoin had a titre of 32 while the other two spider monkeys had titres of 64. Among the captive-born animals the two chimpanzees had titres of 32 and 64 respectively, whereas the two talapoins had titres of less than four. The relevant clinical records from the animal hospital contained no history suggesting clinical measles.

Group 5

Forty-nine of the 61 animals tested initially in group 5 had HAI titres of at least 64. Of these, 27 had titres of 256 or more. Three animals had titres of eight and four animals had no detectable antibody. Paired sera were available from 24 monkeys (Table 2). Among these, 13 showed fourfold or greater rises in titre, diagnostic of currently active infection. Only five of these animals presented clinically diagnostic signs. All had a clearly visible rash over the face, chest and thighs. Two showed in addition respiratory distress with dyspnoea or coughing. Two became very dull, with impaired appetite.

The fifth animal showed a rash only, without other physical signs. Four more

Table 2. *Group 5 animals, bled on two or more occasions*

Date of bleeding ...	HAI titres								
	13.7.76	27.7.76	18.8.76	15.9.76	19.10.76	17.11.76	17.12.76	19.1.77	11.2.77
Animal no.									
146	512	512							
149	512	512							
155	512	256							
156	16	256							
157	256	256							
158	256	256							
159	512	256							
160	256	256							
165	32	256							
166	< 4	256							
169	64	256							
170	32	256							
172	64	256							
180	128	128							
181	64	256	512	512	512	256	256	512	512
182	128	512	512	256	256	128	128	128	128
185	64	256	512	512	512	256	256	512	256
186	64	256	256	512	256	256	256	256	256
189	128	256							
193	256	512	512	512	512	256	256	256	256
194	8	512	512						
196	256	512	256	512	512	256	256	256	256
204	128	512	512	256	512	256	512	512	512
209	64	256	512	256	64	128	256	256	256

of the animals with rising antibody titres showed a superficial stomatitis similar to that reported by Remfry (1976) but visible only on close examination under anaesthesia. In the remaining four animals sero-conversion was not accompanied by any physical signs at all.

Seven animals in group 5 died during or after the outbreak and were autopsied. Large multinucleate giant cells of the type described elsewhere in relation to measles (Warthin, 1931; Finkeldy, 1931; Scott & Keymer, 1975) were found in the lungs in three cases (Plate 1). Cells with numerous large vesicular nuclei (Plate 2), associated sometimes with large intracytoplasmic inclusion bodies, were also plentiful in the lungs in two cases. In contrast to observations by previous workers Warthin–Finkeldy giant cells could not be found in the spleen or lymphoid tissues.

A case of balanitis showed non-specific inflammation of the epidermis of the prepuce, but none of the giant cells of either reticulo-endothelial or epithelial origin described in bronchus and colon by Scott & Keymer (1975). However, the bladder of this animal showed enormous multinucleate giant cells with hyperchromatic nuclei and intensely eosinophilic cytoplasm (Plate 3).

The examination of sera taken from eight monkeys over a period of 7 months from the original measles episode showed a fall in HAI antibody titre in only one instance.

Tests for Influenza A virus CF antibody were also negative, but CMV antibody was present in low titre, suggesting possible earlier exposure to this virus.

DISCUSSION

The virtually complete absence of antibody among the offspring in group 1 supports the view that captive-born monkeys are fully susceptible to measles. Moreover, the antibody titres of imported animals are lower among those resident in England for several years than among recently imported stock (Fig. 1). The geometric mean titre among adults in group 1 together with the whole of group 2 is 33·2 (18·4–59·9), whereas the corresponding values for group 3 animals was 139·3 (104·2–186·2). Comparison by Student's t test shows the difference to be significant ($P < 0{\cdot}1$). If infection occurs near the time of importation, it would appear that antibody drops slowly thereafter, although little change may occur for 6 months or more after infection.

The pattern of results from the initial bleeding of monkeys in group 5 is consistent with recent widespread measles infection of an initially susceptible group. Observations on the 13 sero-converting animals establish that measles in monkeys may be wholly without symptoms (4/13) or marked by signs so slight as to be detectable only by examination under anaesthesia (4/13). This is further supported by the finding of antibody in two captive-born chimpanzees without clinical history of measles.

Mortality from measles in monkeys may vary considerably. During the outbreak described in group 5 there was a total of seven deaths in 72 animals whereas in an outbreak in a group of Abyssinian colobus monkeys (*Colobus guereza*) described by Scott & Keymer (1975) all ten animals died rapidly from the disease. This may reflect the role played by the physical condition of the animals at the time of

infection, as has been suggested in measles in children by Dossetor, Whittle and Greenwood (1977). On the other hand it may represent a true species difference or a difference in the virulence of the infecting strain of virus.

The giant cells found in the bladder of one monkey (Plate 3) were similar to those seen in the bronchial and colonic epithelium in the Abyssinian colobus monkeys mentioned above. Similar cells have been described by Renne, McLaughlin & Jenson (1973) in ectocervix and endometrium of a rhesus monkey artificially infected with measles virus.

Many of the giant cells seen in the lungs in this series had vesicular nuclei and intracytoplasmic inclusions in contrast to the hyperchromatic nuclei of the typical Warthin–Finkeldy giant cells. The cells with vesicular nuclei were more reminiscent of the giant cells of cytomegalic disease than of measles.

Antibody of CMV virus was present at low titres in some of the animals in group 5 six months after the measles outbreak. The significance of this is uncertain. It is unknown how widespread this antibody is in the captive monkey population. Certainly the virus circulates freely amongst humans and the tissue reaction to measles virus in this epidemic may have been modified by an earlier exposure to CMV.

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EXPLANATION OF PLATES

Plate 1

Classical Warthin–Finkeldy giant cell with hyperchromatic nuclei in pneumonic lung. Haematoxylin and Eosin × 500.

Plate 2

Multinucleate cell with vesicular nuclei and intracytoplasmic inclusions in pneumonic lung. Haematoxylin and Eosin × 500.

Plate 3

Multinucleate cells on surface of transitional epithelium in bladder of monkey suffering from balanitis. Haematoxylin and Eosin × 500.