Experimental Kuru in the Gibbon and Sooty Mangabey and Creutzfeldt-Jakob Disease in the Pigtailed Macaque

With a Summary of the host range of the subacute spongiform virus encephalopathies

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Abstract. The experimental host range for the slow virus infections causing subacute spongiform virus encephalopathies is enlarged in primates to include the gibbon for kuru, the pigtailed macaque for Creutzfeldt-Jakob disease, and the sooty mangabey for both diseases. The report is based on neuropathological evidence of the diseases in animals with preclinical lesions. A table lists all the species to which the subacute spongiform virus encephalopathies have been transmitted.

We report subacute spongiform encephalopathy characteristic of experimentally transmitted kuru and Creutzfeldt-Jakob (C-J) disease at a preclinical stage in five primates, comprising a gibbon (Hylobates lar) and a sooty mangabey (Cercocebus atys) with kuru, and a pigtailed macaque (Macaca nemestrina) and two sooty mangabeys with C-J disease.

The previous primate host range for the experimental transmission of kuru and C-J disease consisted of the chimpanzee [8, 12] and four different species of New World monkey: spider monkey (Ateles geoffroyi), capuchin monkey (Cebus sp.), squirrel monkey (Saimiri sciureus), and woolly monkey (Lagothrix lagothica), as summarized previously [9]. More recently, transmission has been reported to the marmoset, Sanguinus sp. [16], member of another family of New World monkey. In one case, kuru was transmitted to a rhesus monkey (Macaca mulatta) after an incubation period of 8.5 years [6]. This animal was the first Old World monkey to show clinical
<table>
<thead>
<tr>
<th>Code No.</th>
<th>Kuru</th>
<th>Creutzfeldt-Jakob disease</th>
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</thead>
<tbody>
<tr>
<td></td>
<td>(Hylobates lar)</td>
<td>(Macaca nemestrina)</td>
</tr>
<tr>
<td>782W</td>
<td>human kuru brain suspension (10% brain suspension)</td>
<td>chimpanzee A-54 (10% brain suspension)</td>
</tr>
<tr>
<td>(U71/146)</td>
<td>spider monkey S-1</td>
<td>human C-J disease</td>
</tr>
<tr>
<td></td>
<td>(10%, 220 nm filt.)</td>
<td>10% brain suspension</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Date</th>
<th>Date of death</th>
<th>Period between inoculation and death, months</th>
</tr>
</thead>
<tbody>
<tr>
<td>Oct. 10, 1966</td>
<td>July 17, 1968</td>
<td>10½</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Code No.</th>
<th>Kuru</th>
<th>Creutzfeldt-Jakob disease</th>
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</thead>
<tbody>
<tr>
<td></td>
<td>(Cercocebus atys)</td>
<td>(Cercocebus atys)</td>
</tr>
<tr>
<td>CFU199</td>
<td>sooty mangabey</td>
<td>chimpanzee A-54</td>
</tr>
<tr>
<td>(U62/69)</td>
<td>(Cercocebus atys)</td>
<td>human C-J disease</td>
</tr>
</tbody>
</table>

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<thead>
<tr>
<th>Date</th>
<th>Date of death</th>
<th>Period between inoculation and death, months</th>
</tr>
</thead>
<tbody>
<tr>
<td>July 17, 1968</td>
<td>Sept. 21, 1968</td>
<td>2½</td>
</tr>
</tbody>
</table>

1 All inocula by intracerebral route.

2 All deaths were due to intercurrent infections (pneumonia and gastroenteritis).
### Table II. Host range of the subacute spongiform virus encephalopathies

<table>
<thead>
<tr>
<th>Primate hosts</th>
<th>Diseases of man</th>
<th></th>
<th>Diseases of animals</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Kuru</strong></td>
<td>aperes: chimpanzees, gibbon&lt;sup&gt;1&lt;/sup&gt; New World monkeys: capuchin, marmoset, spider, squirrel, woolly Old World monkeys: cynomolgus, mangabey&lt;sup&gt;1&lt;/sup&gt;, rhesus, pigtailed, bonnet</td>
<td></td>
<td><strong>Scrapie</strong></td>
</tr>
<tr>
<td><strong>Creutzfeldt-Jakob disease</strong></td>
<td>aperes: chimpanzee New World monkeys: capuchin, marmoset, spider, squirrel, woolly Old World monkeys: African green, baboon, bushbaby, cynomolgus, mangabey, patas, pigtailed&lt;sup&gt;1&lt;/sup&gt;, rhesus, stumptailed, talapoin</td>
<td></td>
<td><strong>Transmissible mink encephalopathy</strong></td>
</tr>
<tr>
<td><strong>Non-primate hosts</strong></td>
<td><strong>Disease of man</strong></td>
<td><strong>creatures</strong></td>
<td><strong>Disease of animals</strong></td>
</tr>
<tr>
<td><strong>Kuru</strong></td>
<td>mink [11&lt;sup&gt;2&lt;/sup&gt;]</td>
<td>gerbil, goat, hamster, mink, mouse, rat, sheep, vole</td>
<td><strong>Scrapie</strong> [10]</td>
</tr>
<tr>
<td><strong>Creutzfeldt-Jakob disease</strong></td>
<td>cat [7], guinea pig [14]&lt;sup&gt;2&lt;/sup&gt;, mouse [2]&lt;sup&gt;2&lt;/sup&gt;</td>
<td>ferret, goat, hamster, mink</td>
<td><strong>Transmissible mink encephalopathy</strong> [4, 5, 13]</td>
</tr>
</tbody>
</table>

<sup>1</sup> By pathology only.

<sup>2</sup> Unconfirmed.
evidence of kuru. Subsequently, transmissions have been made to other Old World monkeys [10]. The current list of all host species, which includes the mink and the domestic cat, is given below.

In table I the five primates to which we report transmission of kuru or C-J disease and the pertinent experimental details are recorded. In all of these cases transmission was demonstrated not by clinical disease, but by characteristic pathology during the preclinical (incubation) period of the disease. The discovery of preclinical lesions in the brain is in accord with EEG changes described in a chimpanzee at five months’ postinoculation, before the onset of clinical disease [3], and with a study carried out in spider monkeys [1]. A full account of the neuropathology of the preclinical lesions is reported elsewhere [15]. Because the features of neuronal vacuolation, fibrous astrocytosis and status spongiosus are pathognomonic of the subacute spongiform encephalopathies, preclinical diagnosis can be made with confidence. Subsequently, transmission of clinical disease has been effected for C-J disease in the sooty mangabey; but for experimental kuru in the gibbon and sooty mangabey and C-J disease in the pigtailed macaque, the sole evidence for transmission so far is histopathological.

The primary purpose of this communication is to report the transmissions of the subacute spongiform encephalopathies to these new host species, which represents a significant extension of their host range. In addition, the full experimental host range, in our current state of knowledge, is summarized in table II [2, 4, 5, 7, 11, 13, 14]. It is now evident that kuru and C-J disease can be passaged to representatives of all anthropoid families, and, with transmission effected to the gibbon, to both subfamilies of pongids. The search for a less expensive host with a shorter incubation period has resulted in kuru being transmitted to the mink [11] and C-J disease to the cat [7] and probably the guinea pig [14] and mouse [2], and this should be of considerable assistance in pursuing the nature of the infectious agents.

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