

SHORT REPORT

Transmission of Creutzfeldt-Jakob disease to a chimpanzee by electrodes contaminated during neurosurgery

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Abstract

Stereotactic multicontact electrodes used to probe the cerebral cortex of a middle aged woman with progressive dementia were previously implicated in the accidental transmission of Creutzfeldt-Jakob disease (CJD) to two younger patients. The diagnoses of CJD have been confirmed for all three cases. More than two years after their last use in humans, after three cleanings and repeated sterilisation in ethanol and formaldehyde vapour, the electrodes were implanted in the cortex of a chimpanzee. Eighteen months later the animal became ill with CJD. This finding serves to re-emphasise the potential danger posed by reuse of instruments contaminated with the agents of spongiform encephalopathies, even after scrupulous attempts to clean them.

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More than 15 years ago, Creutzfeldt-Jakob disease (CJD) was accidentally transmitted to two young people by stereotactic electroencephalographic (SEEG) exploration with multicontact probe electrodes that had previously been implanted in the brain of a middle aged patient with familial presenile dementia and myoclonic jerks.¹ The electrodes apparently remained contaminated with the infectious agent of CJD despite attempts to sterilise them with alcohol and formaldehyde vapour. The purpose of this communication is to document that the diagnoses of all three patients have been confirmed by transmission of disease to animals and to describe the transmission of CJD to a chimpanzee by

implantation of the same electrodes used in the two iatrogenic cases after sterilisation and storage in formaldehyde vapour for two years after their last use in humans. We failed to transmit disease to another animal, the brain of which was implanted with gold wire electrodes that had been glued to the scalps of the three patients and then cleaned with the same regimen used for the silver electrodes.

Methods and results

In September 1974, two multicontact depth electrodes (probe electrodes with multiple silver contacts separated by rings of insulating plastic) were used to explore the cerebral cortex of the source patient with CJD, and SEEG recordings of electrical activity were conducted at various depths in the cortex, subcortical white matter, caudate nucleus, and ventrolateral thalamus to select suitable sites for brain biopsy and thermocoagulation. The electrodes were in place for about two hours after which they were removed, cleaned with benzene, disinfected with 70% ethanol, and placed in a preautoclaved metal box containing a formaldehyde generator (2 g paraformaldehyde) where they were stored for two months. In November 1974 the two silver electrodes were implanted for a period of several hours in the cerebral cortex of a 23 year old woman with drug resistant psychomotor epilepsy, after which they were again cleaned, sterilised, and stored as described. In December 1974 these same silver electrodes were implanted for a period of several hours in the cortex of a 17 year old boy with postencephalitic psychomotor epilepsy. After their last use, the two silver electrodes were again decontaminated and sterilised as before and left in the formaldehyde vapour sterilising container for the next two years. As previously reported¹ both patients subsequently developed progressive neurological disease, the young woman (iatrogenic case 1) 20 months and the young man (iatrogenic case 2) 16 months after the SEEG procedures. Both patients died, and the diagnoses of CJD were confirmed by histopathology at necropsy as well as by inoculation of brain suspensions into primates, which subsequently developed progressive neurological disease typical of spongiform encephalopathy (table).

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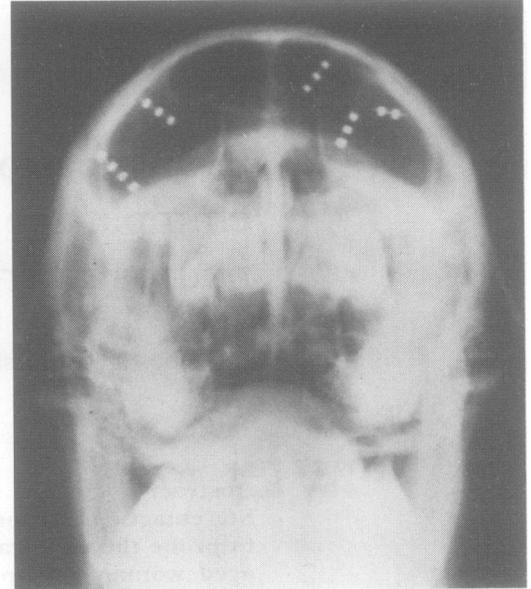
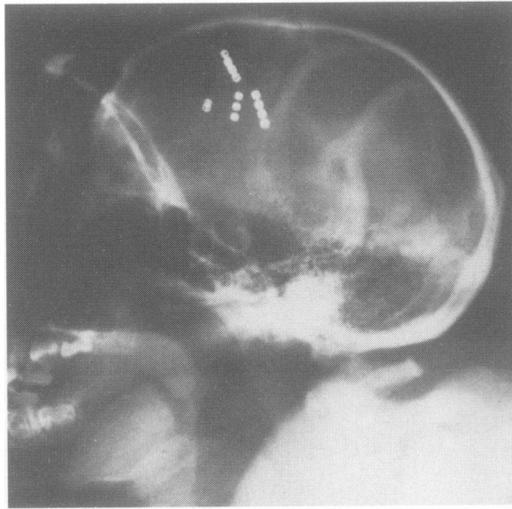
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Encephalopathy in animals inoculated with materials from patients with CJD involved in iatrogenic electrode transmission

Iatrogenic case identification	Inoculum	Animals inoculated			Survival (months)	
		Species	Number	CJD	Range	Average
Source patient Case 1	Electrodes (Ag)	Chimpanzee	1	+	20	
	Brain 10%	Rhesus monkey	1	+	75	
	Brain 10%	Squirrel monkey	1	+	18	
	Brain 10%	Guinea pig	1	0	40	
Case 2	Brain 10%	Capuchin monkey	2	+	38-39	39
	Brain 10%	Chimpanzee	1	+	11	
	Brain 10%	Squirrel monkey	4	+	16-27	23
	Brain 10%	Vervet monkey	2	+	46-67	57
Case 2	Electrodes (Au)	Chimpanzee	1	0	> 195	

All animals were inoculated intracerebrally; Ag = silver multicontact depth electrode; Au = gold scalp electrodes; + = animal(s) died with spongiform encephalopathy; 0 = animal still alive or died of other cause.

Radiographs showing lateral (left) and frontal (right) views of the skull of a chimpanzee after cortical implantation of multicontact depth electrodes accidentally contaminated with the agent of CJD.



The electrodes were then sent to our laboratories at the National Institutes of Health. On 13 January 1977 (28 months after their use in the original CJD case) the electrodes were divided into five segments and inserted through burr holes into the brain of a juvenile male chimpanzee, two segments into the right frontal lobe, and three segments into the left frontal lobe (fig). The burr holes were then filled with bone wax and the subcutaneous tissues were closed with chromic sutures. (Anesthesia and aseptic surgical technique were used throughout.) The procedure was tolerated well, and the animal remained asymptomatic for more than a year.

Eighteen months after the electrodes were implanted, the chimpanzee showed signs of encephalopathy. Neurological disease became more severe during the next seven weeks. When the animal was incapacitated it was anaesthetised deeply, exsanguinated, and a necropsy examination was carried out. Changes of spongiform encephalopathy—pronounced vacuolation and proliferation of astrocytes—were found in many areas of the brain.

Several small gold wire electrodes that had been used to map the horizontal extent of epileptic activity on the scalps of each of the patients and cleaned and sterilised in the same manner as the depth electrode were also inoculated through burr holes into the frontal cortex of another chimpanzee. That animal remains well more than 16 years after the procedure (table).

Discussion

CJD, kuru, and scrapie are caused by infectious pathogenic agents that are uniformly lethal but apparently of low contagion.² Were that not the case, we should expect to have found a higher incidence of CJD in medical personnel most at risk, spouses of patients,

and morticians. In an analysis of more than 2000 case histories we found no suggestion of a higher frequency of CJD in any such group.³ On the other hand, CJD has been diagnosed in a neurosurgeon and two histopathology technicians, one of whom had documented exposure to the brain of a patient with the disease.⁴ The iatrogenic transmission of CJD—by the SEEG electrodes described here¹ as well as by other neurosurgery, corneal grafts, dural transplants, and injections of hormones extracted from human pituitary glands^{4,5}—remains the only identified mechanism by which infection has been transmitted to people.²

Our findings serve to re-emphasise that stringent care must be taken when decontaminating and sterilising non-disposable equipment used in invasive procedures on patients with CJD or likely to be incubating CJD.⁶ It may not always be possible to sterilise delicate instruments or those having crevices once they are contaminated with the spongiform encephalopathy agent.

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