core ideas about the content and design of the questionnaire. Sarah Ayers (National Perinatal Epidemiology Unit) designed the computer databases and dealt with all computing issues. Jo Garcia, Rona McCandlish, Sally Marchant, Valerie King, and Kirstie McKenzie-McHarg commented on the questionnaire design and drafts of the paper. Suzanne Williams, Sarah Bowler, and Hedwig Van Asten entered the data. AM and NK are guarantors for the paper.

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Claude Bernard on the action of curare

Claude Bernard (1813-78) was professor of experimental physiology in Paris. Among many original observations he was the first to elucidate the "fonction glycogénique" of the liver and invented the term "milieu intérieur."

The following is an abridged version, which I have translated, of "Physiological studies on certain American poisons," first published in *La revue des deux mondes* in 1864.

"Curare has been known since its discovery in Guyana by Walter Raleigh in 1595. Raleigh reported on this poison in Europe, used on poisoned arrows, under the name 'Curari.' The symptoms of death from curare, all observers agree, are quite characteristic.

"Watterton has described the death of a man poisoned by curare. Two Indians were hunting for game in the forest. One of them took a poisoned arrow and shot it at a red monkey which was above him in a tree. The direction of the arrow was almost perpendicular. The arrow missed the monkey and in falling hit the Indian on the arm just above the elbow. He was convinced that all was finished. 'Never,' he said to his companion in a broken voice, and looking at his bow while he spoke, 'will I bend this bow again.' Having spoken these words, he removed from his shoulder the small bamboo box which contained the poison, and having placed his bow and arrows on the ground, he lay down, said goodbye to his companion, and never spoke again. 'It will be a consolation for tender souls,' remarked Watterton, 'to know that the victim did not suffer, because 'wourali' takes life gently.

"In June 1844 I made my first experiment with curare: I inserted under the skin of the back of a frog a small piece of dry curare, and observed the animal. Initially, the frog moved and jumped around with great agility, then it became quiet, the body became flat and gradually subsided. After several minutes the frog was dead, that is to say, that it had become limp, and pinching the skin produced no reaction. I then proceeded with what I call a 'physiological autopsy' on the animal. Sensible regulations, widely approved, prevent one from doing an autopsy on the human until 24 hours have elapsed since death. These circumstances

detract considerably from the scientific importance of the 'cadaveric autopsy'....

"It is different, as one will see, when one does an autopsy physiologically, that is to say, by opening the body immediately after death. Man has the right to use animals for domestic purposes and for food, and has equally the right to use animals to inform himself scientifically in a manner useful to humanity.

"On opening the poisoned frog, I saw that its heart continued to beat. Its blood became red on exposure to the air and appeared physiologically normal. I then used electrical stimuli as the most convenient method of provoking a reaction in the nerves and muscles. Stimulating the muscle directly produced violent contractions in every part of the body, but on stimulating the nerves there was no reaction. The nerves, that is, the bundles of nervous tissue, were completely dead, while the other bodily components, the muscles, the blood, the mucous membranes, retained their physiological properties for a number of hours, as one sees in cold blooded animals....

"If the heart retains its power of movement, this proves, what one already knew, that it is not influenced by the nervous system as are the other muscles.

"That first analytical experiment on the frog was later repeated on a number of animals more closely related to man and belonging to the classes of birds and mammals. I have found identical results, and the 'physiological autopsy' showed me that, as in the frog, the motor nerves are the only tissues affected by curare, while the other components of the body retain their physiological properties."

Bernard was, of course, wrong in his interpretation; his pupil Vulpian suggested that curare acted on the motor endplate, whose morphology had been recently described by Kühne.

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