

The Jezierski papers: live polio vaccine development in colobus monkey cells but not chimpanzee cells in the Belgian Congo, 1952–1958

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A reading of ten relevant papers by Alexandre Jezierski provides evidence for the only attempt in Central Africa to develop a live oral polio vaccine (OPV) from growing reference wild polio strains to 210 passages in colobus monkey tissue culture, and experimental administration to about 25 humans. Chimpanzees were used as a human model, but their tissues or kidneys were absent from the passage and production line of the proposed vaccine. Thus, the implication published by Hooper that Jezierski had produced a candidate OPV that might have contained chimpanzee viruses, possibly simian immunodeficiency virus cpz or the precursor of human immunodeficiency virus-1 group M, is incorrect.

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1. INTRODUCTION

Alexandre Jezierski, born in 1909 in Poland, became a veterinarian in his native country, and was in Western Europe when the war broke out in 1939. He obtained a PhD in Berne, Switzerland. He was employed by the veterinary laboratory service of the Belgian Congo in 1947, and stationed at the veterinary laboratory of Elisabethville (now Lubumbashi). He was detached from the colonial government service in 1951–1952 to work with the powerful INEAC (Institut National pour l'Etude Agronomique du Congo Belge) agronomy research agency. They sent him to the veterinary station at Nioka, near Lake Albert and Uganda, 800 km from the provincial capital of Stanleyville (Kisangani) and 900 km from the headquarters of INEAC at Yangambi. He was appointed head of the INEAC veterinary laboratory in Gabu, 7 km from central Nioka. He immediately started a strong tissue culture laboratory, centring on polio, although this was not his or INEAC's remit. He received help initially from the Institut Pasteur, Paris. He had ample freedom to go and see techniques internationally, and he made the best use of the mandatory leave of six months imposed every three years by the colonial government and INEAC on non-African employees. In 1958, he was made redundant by the INEAC and returned to the government veterinary laboratory service in Elisabethville. After Congolese independence (30 June 1960), he stayed on duty until he was offered a position by the United Nations Food and Agriculture Organization headquarters in Rome in 1964. He resided in Spain and in Brussels where he died in 1991, before the 'oral polio

vaccine (OPV) theory of acquired immune deficiency syndrome' gained notice. He had not worked on polio since 1958. His ten relevant papers were published during 1950–1960 (Delville & Jezierski 1950; Jezierski & Delville 1950*a,b*; Barski *et al.* 1954; Jezierski 1955*a–c*, 1959, 1960; Jezierski & Adriaensen 1959). He had few co-authors, all now deceased.

2. THE ELISABETHVILLE PAPERS

These papers describe attempts to isolate, by serial passage and various routes in various animals, an agent from paralysis in: a dog suspected of rabies (Delville & Jezierski 1950); stool of a child with transient paralysis of the palate (Jezierski & Delville 1950*a*); and swine from an epidemic with many survivors (Jezierski & Delville 1950*b*).

The outcome was that the 'agents' ended by killing most animal species, including monkeys and two chimpanzees. Jezierski never looked back at these papers, but according to his co-author J. Delville from the medical laboratory and veterinarian J. Mortelmans (personal communication), rabies has been diagnosed in the US in the Jezierski materials. He may have missed the Negri bodies, if any. Jezierski obviously had learned that laboratory cross-contamination is a serious threat, and that one needed the new tissue culture to do animal or human virology.

3. *IN VITRO* HOST RANGE OF POLIO VIRUSES: WITH THE INSTITUT PASTEUR AND GOING ALONE AT NIOKA

In all the Jezierski papers, the only polio type 1, 2 and 3 viruses are three international wild prototype strains

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given to him by the Institut Pasteur, or their derivatives by passage. He was indebted to the Institut Pasteur for training, for visits by G. Barski, and for monetary support whether directly or by influencing INEAC. It is not clear what part of his 1954 paper (Barski *et al.* 1954) was done in Paris or in Nioka, but the Nioka part must be substantial. Together with a 1955 paper (Jezierski 1955*a*), it shows that explant cultures—mainly from testicles, and also kidneys and other organs—from all of 14 Congo non-human primate species were susceptible to polio viruses, with the only exception of lemurs. This array of susceptible primate species in a single country is impressive, but it was not unexpected in 1949–1950, when Old World primate cultures, mainly from Asia, all did well.

This 1955 paper (Jezierski 1955*a*) is the first mention by Jezierski of chimpanzee cultures being susceptible to polio viruses. The organ and the number of chimpanzees is not specified here and only the principle was established. All chimpanzees used by Jezierski were probably *Pan troglodytes schweinfurthii*.

In hindsight this 1955 paper on host range is the only proof of his use of chimpanzee tissue cultures.

In a footnote to this 1955 paper, Jezierski mentions without explanation that he has observed ‘attenuation’ of wild polioviruses on *Colobus* sp. cultures.

4. JEZIERSKI'S FIRST VACCINE PAPER

There are no chimpanzees in the first vaccine paper (Jezierski 1955*b*). Wild prototype viruses were grown in *Cercopithecus* tissue culture, and tested for inactivation by formalin on cercopithecus and colobus cultures. Both species were used for vaccination attempts by subcutaneous, intramuscular and intracerebral routes.

After 21 passages of wild-type viruses in colobus cultures only, injections were given to cercopithecus and cercocebus monkeys only. *In vitro* testing was as for inactivated vaccine. The results looked promising.

5. COLOBUS-DERIVED OPV INTO CHIMPANZEES

Wild-type polio 1, 2, 3 was serially passaged 210 times in colobus cultures, 1–60 times in organ explants and 61–210 times in trypsinized kidney cultures. Neurovirulence was tested in cercopithecus (Jezierski 1959). All *in vitro* tests were on cercopithecus and colobus cultures. Twelve chimpanzees were fed with passage 148. All parameters were satisfactory. No chimpanzees was sacrificed, and there were no chimpanzee tissue cultures. One chimpanzee was tested intracerebrally for neurovirulence, and was negative.

6. COLOBUS PASSAGE 148 OPV IN 21 HUMANS, 'A BRIDGE TOO FAR'

Following administration of colobus passage 148 OPV to 21 humans no viraemia or disease was found, vaccine virus was in stool for up to seven weeks and neutralizing antibody appeared in most (Jezierski & Adriaensen 1959). *In vitro* tests were as in §§ 4 and 5.

This seemed excellent, but that's not how veterinarians should conduct human trials—single-handedly in a one-physician hospital. Jezierski was removed from polio work during his leave in Belgium in 1958.

7. POLIO IMMUNOGLOBULIN IN DONKEYS, AND ITS ORAL USE IN CHIMPANZEES AND HUMANS

Jezierski (1955*c*) is about injecting donkeys with collected supernatants from polio cultures in monkey tissue culture and the resulting high-titre antibody. After preparation of hyperimmune immunoglobulin by standard methods, it had a higher seroneutralization titre than reference Lederle immunoglobulin. All assays were on monkey cells, not chimpanzee cells.

In 1960, Jezierski reported an unorthodox attempt to use the oral route with the hyperimmune globulin, trying to clear the gut of chimpanzees from colobus-attenuated poliovirus (Jezierski 1960). After immunity had been established, virulent prototype strains were also used. The number of chimpanzees, always used as whole animals, is not specified here. A similar experiment was added with international prototype attenuated viruses; here, 16 chimpanzees were used. The substrate for *in vitro* testing is not specified, but it should have been monkey kidney (colobus, cercopithecus...) as usual, not chimpanzee cells.

The same paper carries a critique by J. Mortelmans and P. Brutsaert, suggesting that the ‘destruction’ of poliovirus by ingested immunoglobulin was far from complete. Brutsaert added: ‘It is clear that an isolated man, however capable and hard-working he is, is unable to collect all necessary controls and reagents for this size of enterprise!’. Brutsaert suggests that Jezierski should interest a big laboratory in Europe or in America in his work, meaning that this had not been done since the initial contact with the Institut Pasteur. In his rebuttal and final comment, Jezierski complains that he had been prevented from finishing work and bringing his full notes from Gabu Nioka. He adds a number of incomplete experiments that do not clarify much.

In all, Jezierski seems to have used about 25 people for experiments with his colobus-derived vaccine, and about 30 chimpanzees.

8. JEZIERSKI AND POLIO: AN APPRECIATION

Jezierski may have used about 30 chimpanzees for the polio work at Gabu Nioka. He let them survive. He described chimpanzee tissue culture only once (Jezierski 1955*a*) to show that in principle their tissues were equally suitable for polio growth as those of other Congolese primates.

Jezierski, like other scientists, never calls a chimpanzee a ‘singe’ or a monkey, only a chimpanzee. They all had given names.

Jezierski never used chimpanzee tissue culture in the passage or production line of his candidate killed live polio vaccines. The live vaccine was derived from colobus tissue culture only, with kidney trypsinization used from passages 61 to 210.

The colobus-derived vaccine seemed valuable, but Jezierski was not in a position to experiment with it safely in about 25 humans. The INEAC and the colonial authorities had no choice but to dissuade Jezierski from solitary polio work, which they started to do

formally in 1955. He was removed from all polio work and from Nioka in 1958, apparently without any safety incident.

Colobus monkeys were the most abundant monkeys in Nioka. They are ornate and they were valued for their skin. Jezierski was a reputed marksman. His colobus were shot and immediately used, with rare exception. They were not suited for captivity because of their reliance on fresh (ironwood) leaves. Perhaps Jezierski liked the idea of making an exclusive vaccine that could not be repeated elsewhere, except in colobus-rich habitats.

According to all testimonies and documents, Jezierski was an 'impeccable' scientist doing his experiments himself with a small core of tightly steered employees. He fell out with almost all colleagues and peers at and above his hierarchical level, but no one accused him of bad science. Contrary to the claims of Hooper (1999), interactions with scientists outside his work place were very limited. Nobody found him an attractive personality to deal with easily.

The Jezierski papers are not a fraud, not as far as a virologist can tell. Some precision we would like today is lacking in his papers, but this is not different from other 1950–1960 literature.

From INEAC and initially perhaps from the Institut Pasteur, Jezierski had the financial means to do what he described. He single-handedly turned Gabu Nioka into a laboratory doing difficult tissue culture, virology, and polio vaccine development. He sacrificed many monkeys, but not chimpanzees.

Finally, the Jezierski vaccines could not have contained simian immunodeficiency virus cpz, since there were no chimpanzees in their passage and production line.

Jezierski in Gabu Nioka made the only attempt in Africa to develop an OPV from wild strains to experimental vaccines, with the exception of South Africa. He and his papers should be remembered for this, not for having set the scene for spreading chimpanzee viruses through vaccines. This has never happened anywhere, in spite of the beliefs of Hooper (1999).

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