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SIMIAN VIRUSES AND POLIO VACCINES

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It was the development of cell culture techniques that proved decisive for the successful production of polio vaccines in the 1950's. The use of kidney cell cultures from different monkey species permitted the replication of poliovirus *in vitro*. Over years of working with these cell cultures, it has become apparent that the monkey cells might be contaminated with various known or previously unknown viruses. In two cases the discovery of new viruses from monkeys with latent infections has attracted special attention. These are the simian virus 40 (SV40) and the simian immunodeficiency virus (SIV). The idea that these viruses could be transmitted by polio vaccination and possibly cause disease has been the subject of discussion both in professional circles and in the mass media.

SV40

SV40 is a small, very stable DNA virus related to papilloma virus. SV40 occurs naturally in certain Asian macaque monkey species, especially in rhesus monkeys, and was discovered in 1960. In 1962 it was reported that the new virus could induce tumours in newborn hamsters and provoke malignant transformation of human cells *in vitro*. At the same time it was shown that non-inactivated, infectious SV40 was present as a contaminant of inactivated poliovirus vaccines (IPV) throughout the world. In the USA it has thus been estimated that somewhere between 10 and 100 million Americans have been vaccinated with IPV containing non-inactivated SV40. Infectious SV40 was also demonstrated at that time in test samples preserved from IPV produced at Statens Serum Institut in Denmark. It must be regarded as probable that IPV used for vaccination in Denmark during the period April 1955 to around New Year 1964 could have contained SV40. Since then the vaccine has been known to be free from SV40, because once the possibility of contamination was realized, all IPV produced has been tested for the virus. Live oral poliovirus vaccine (OPV) was first used in Denmark in the campaign of April-May 1963. The vaccine used on that occasion was probably not contaminated, and the OPV used in the campaigns of 1966 and later in the Danish childhood vaccination programme has been known to be free from SV40. During the 1990's several reports have appeared showing traces of SV40 in cells from certain types of cancer. These are SV40-like DNA sequences and SV40-specific antigen, found in tumour cells from some mesotheliomas, ependymomas, choroid plexus tumours and osteosarcomas. The question is whether the virus has contributed to the development of the tumours, or whether its presence is a random finding of no significance. If the former possibility is true, it raises the further question of whether the polio vaccines given about 40 years ago could have contributed. Current evidence does not support such a connection. In the first place, many of the tumours in which traces of SV40 have been demonstrated are from patients that were born several years after the period in which SV40-contaminated vaccines were used. Secondly, several epidemiological studies have been carried out in which cohorts that were vaccinated with contaminated polio vaccine have been compared with cohorts that were not. In such large studies from the USA, Germany and Sweden, the incidence of cancer has been followed for up to 30 years after the vaccinations. These studies have revealed no evidence that SV40-contaminated IPV or OPV has caused an increased incidence of cancer, nor with respect to the particular forms of cancer mentioned above. Similar studies are being planned in Denmark.

SV40 antibodies have been demonstrated in a small percentage of the US population. However, a similar prevalence of SV40 antibodies has also been found in collections of human serum samples taken several years before the introduction of polio vaccine in 1955.

Conclusion

The idea that SV40-contaminated polio vaccine could have contributed to the development of human cancers is purely hypothetical. The available evidence provides no support for this theory. From 1964 onwards the Danish vaccination programme has not been affected by SV40 contamination.

SIV

The origin of the AIDS epidemic has been the object of much speculation. According to one much-debated theory, the HIV-1 epidemic can be traced back to certain experimental OPV vaccinations carried out during 1957-59 in the former Congo. The OPV used is supposed to have been contaminated with SIV from chimpanzee kidney tissue. After transmission to man, SIV is then supposed to have developed over a period of time into HIV-1. This theory was discussed at a meeting in London in September 2000. However, apart from the circumstance that the AIDS epidemic presumably originated in Africa, it is difficult to find evidence to support the hypothesis. Meanwhile, there are several arguments against it. Despite numerous tests, it has never been possible to demonstrate the presence of SIV in OPV. This may relate to the fact that it has also proved impossible to replicate SIV in the cell cultures used to produce OPV. Independent laboratories have recently performed tests on the OPV that was used in the Congo in 1957-59. Sensitive tests for SIV and HIV were negative. In addition, it is note-worthy that remains of mitochondrial DNA could be detected in the vaccine, and it was possible to demonstrate that this originated from macaque monkey cells and not from chimpanzee cells. This seriously weakens the proposed theory, as HIV-1's closest relative among the SIVs from different simian species is clearly the SIV from chimpanzees. Furthermore, several recent genetic studies on HIV-1 indicate that this virus has a history that stretches back to around 1930 or earlier, i.e. many years before the development of polio vaccines. In contrast to SV40, SIV is more sensitive to formaldehyde inactivation than poliovirus. IPV has therefore not been suspected of containing infectious SIV.

Conclusion

It seems unlikely that the HIV-1 epidemic could have arisen as a result of polio vaccinations. Transmission of SIV from ape to man could have occurred in many other ways in Africa.

(K. Bro-Jørgensen, Dept. of Med.)

21 February 2001

Patients with confirmed Listeria monocytogenes infections

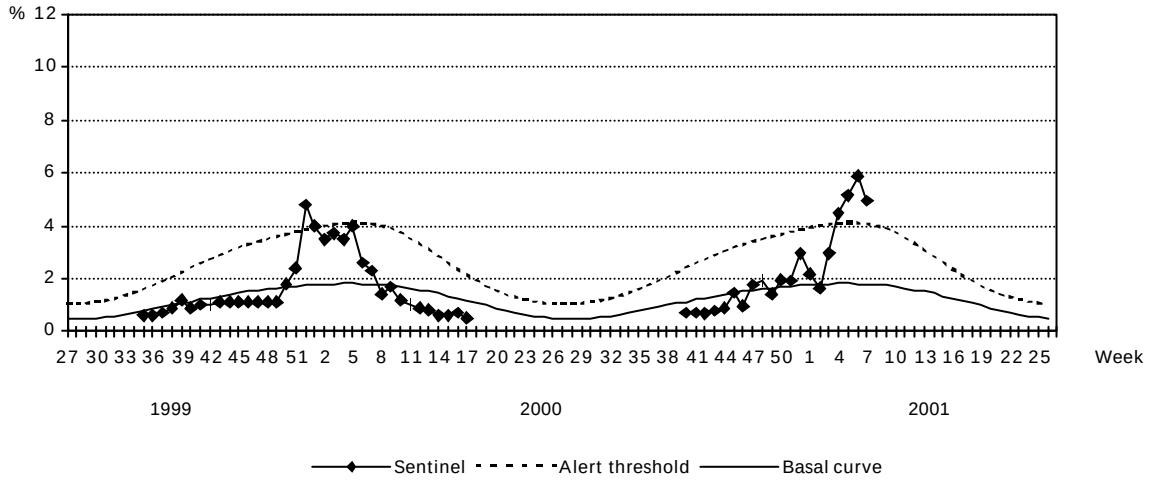
4th quarter of 2000 compared with 1999 (whole year)

	4th quarter 2000	Cumulated 2000	Whole year 1999
Mother/child infection	1	7	3
Septicaemia	5	24	30
Meningitis	2	8	7
Other	0	0	4
Total	8	39	44

(Dept. of Gastrointestinal Infections)

Sentinel surveillance of influenza activity

Weekly percentage of consultations, 1999/2000/2001



Sentinel: Influenza consultations as % of total consultations

Basal curve: Expected frequency of influenza consultations under non-epidemic conditions

Alert threshold: Possible incipient epidemic

Sentinel surveillance is still indicating a high incidence of influenza.

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