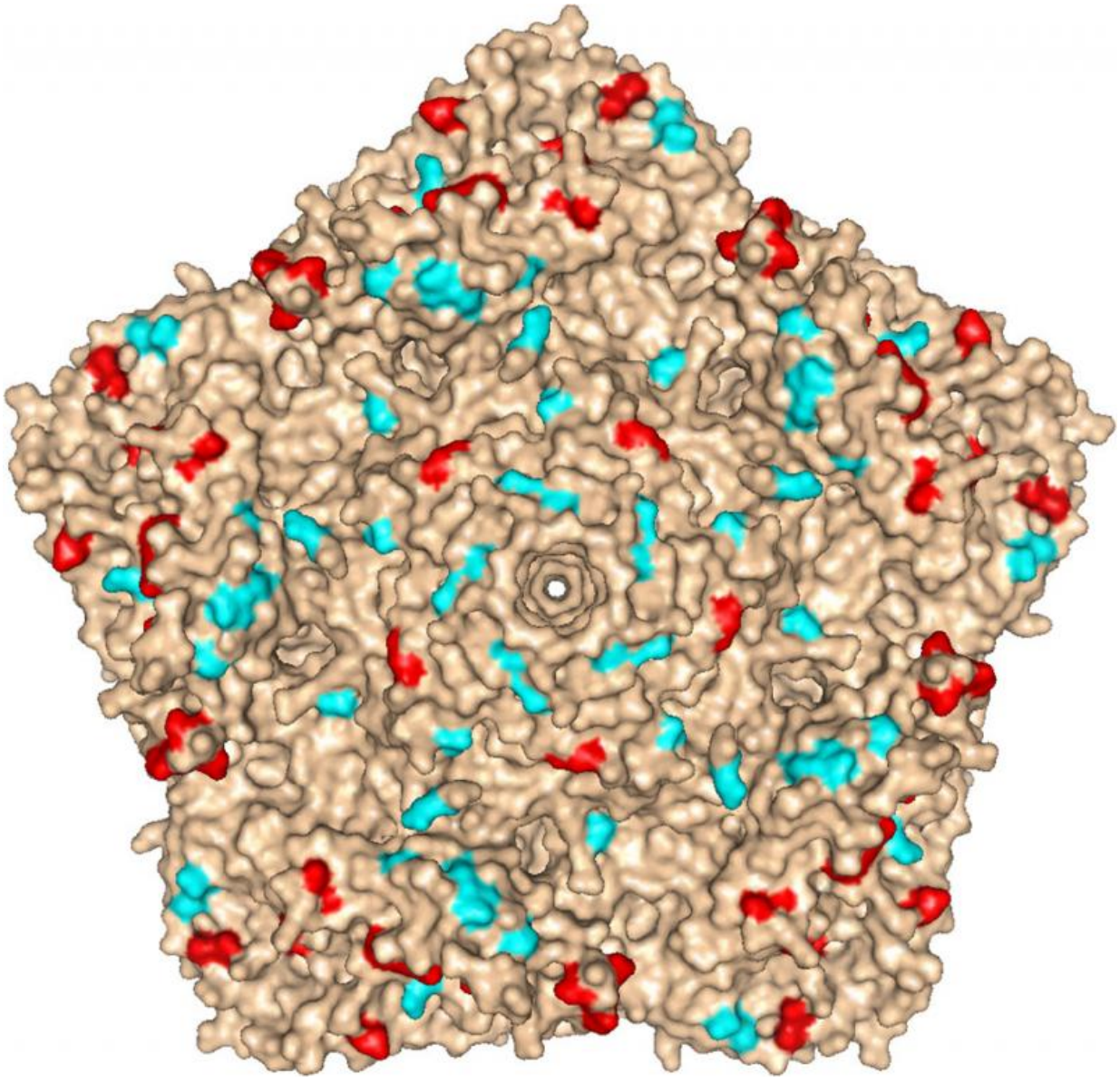
MedicalXpress

A patient shedding poliovirus for 28 years: Possible challenges for polio eradication

August 27 2015



A molecular surface diagram of the three-dimensional structure of type 2 wild poliovirus strain Lansing viewed from the outside of the virion [25]. A pentameric unit is represented. The virus particle consists of 60 protomers. Each protomer contains a single copy of VP1, VP2, VP3, and VP4 arranged in icosahedral symmetry. The location of mutations found in known antigenic sites of iVDPV isolate 160198 with respect to Sabin 2 vaccine strain are shown in red, other amino acid changes from Sabin 2 are displayed in cyan. The image was generated using PyMOL Molecular Graphics System, Version 1.7.0.3 software (Schrödinger, LLC)

With all but two countries worldwide, Pakistan and Afghanistan, declared polio-free, the eradication of the devastating viral disease in the near future is a real possibility. A study published on August 27th in *PLOS Pathogens* reports results from an individual in the UK with an immune disease whose stool samples have contained large amounts of live polio virus for over 20 years. Patients like this one, the authors suggest, could start new polio outbreaks and complicate polio eradication as currently planned.

There are three strains of wild polio virus (1, 2, and 3) and two different types of polio vaccine. Inactivated polio vaccine (IPV) is safe and effective in inducing neutralizing antibodies that protect against paralytic polio. It does not, however, induce substantial mucosal immunity and so prevent excretion of virus. Oral polio vaccine (OPV; which contains weakened, or "attenuated" live virus) is effective, and besides neutralizing antibodies induces mucosal immunity, thereby killing viruses in the gastro-intestinal tract and reducing excretion. OPV is less safe than IPV; on extremely rare occasions, it causes vaccine-associated paralytic polio, and because some shedding into the stool still occurs, it can also lead to circulating vaccine-derived polioviruses (cVDPV).

Over 90% of such cVDPV are due to the strain 2 component, which has

not been seen in the "wild" since 1999 and thus appears eradicated. As strain 2 OPV is also responsible for up to 38% of vaccine-associated paralytic polio cases, WHO plans to implement shortly a switch from trivalent OPV (containing strains 1,2,3) to bivalent OPV (containing only strains 1 and 3) in routine immunization programs. Following eradication, the plan is to stop use of all OPV in routine immunizations, while IPV immunizations are likely to continue for some time.

In this study, Javier Martin, from the National Institute for Biological Standards and Control, Potters Bar, UK, and colleagues, analyzed more than 100 stool samples collected between 1995 and 2015 from a white male. The individual received a full course of childhood immunizations, including OPV at 5, 7, and 12 months, with a booster at about 7 years of age. He was later diagnosed with an immunodeficiency, which can affect the ability of the immune system to kill viruses in the digestive tract.

The researchers found high levels of strain 2 polio virus in all stool samples analyzed. Analysis of the RNA of these iVDPV strains (i.e. strains of vaccine-derived polio virus from immune-deficient individuals) showed that the excreted viruses were different from the weakened vaccine strain, and that they had started to diverge from it an estimated 28 years ago, around the time of this individual's last known vaccination with OPV. All iVDPV strains had mutations that reversed the attenuating features of the vaccine strain, and over time they also acquired a range of other mutations, many affecting the antigenic structure of the virus. All tested iVDPV samples were able to cause paralysis in transgenic mice that had a human poliovirus receptor.

Despite the extensive changes found in the iVDPV strains compared with the vaccine strain, the researchers found that human sera readily neutralized even the most divergent strain—reassuring results, they say, "in that they indicate that vaccinated humans are well protected against infection with these highly drifted iVDPV strains". However, they also

state that "because the sera tested correspond to a selected group of UK healthy adults between 28-65 years of age who had been vaccinated with a full course of four OPV doses plus at least one dose of IPV, whereas the UK switched from OPV to IPV for polio immunization in 2004, it would be helpful to test sera from cohorts that have only received IPV".

Putting the research into context of other studies on iVDPV, they emphasize that "of the total of 73 iVDPV cases that have been described between 1962 and 2014, only seven involved infections lasting more than five years. The case described here represents by far the longest period of excretion described from such a patient and the only identified individual known to be excreting highly evolved vaccine-derived poliovirus at present". However, the researchers also mention that several highly mutated VDPV strains that showed molecular properties typical of iVDPVs have recently been isolated from sewage samples in Slovakia, Finland, Estonia, and Israel, suggesting that an unknown number of chronic excreters exist elsewhere.

The researchers conclude that "enhanced surveillance including sewage sampling and stool surveys to search for the presence of iVDPV strains and the development of efficient anti-viral treatments to interrupt virus replication in immune-deficient individuals are needed to be able to identify and manage the possible risks of iVDPV strains spreading and causing disease in patients and the general population, particularly in the light of changes in vaccination strategies as part of the polio eradication endgame and the absence of an established outbreak response strategy". They add that "new polio vaccines such as those based on non-infectious virus-like particles or even new genetically designed stable live-attenuated versions with no associated risk of producing VDPVs, might be required to complete polio eradication".

More information: Dunn G, Klapsa D, Wilton T, Stone L, Minor PD, Martin J (2015) Twenty-Eight Years of Poliovirus Replication in an

Immunodeficient Individual: Impact on the Global Polio Eradication Initiative. PLoS Pathog 11(8): e1005114. DOI: 10.1371/journal.ppat.1005114