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Abstract	:	Human and animal infections with Orthopoxvirus have become more prevalent in recent years. Although smallpox has been eradicated, vaccinations continue to play a role in controlling the spread of Orthopoxvirus diseases. First generation vaccines were successfully commercialized, and they were widely used previously. Besides, several second-generation vaccines that emphasize sterile cell culture techniques for vaccine production have been developed. Some of the third-generation vaccines also successfully trigger immune responses in the host, and they are being researched as safer substitutes for smallpox vaccines. Extensive work is still being done on the creation of fourth-generation smallpox vaccines, which include the creation of DNA subunit vaccines. Clinical studies must be conducted to evaluate the efficacies of these vaccines. Vaccine was effective in preventing smallpox infection. To achieve the Sustainable Development Goals of the United Nations, a new paradigm for vaccination research and product development must be established.