Roll up your sleeves. Do you see a dime sized pock-mark scar on your upper arm? If not, then odds are, you are under 50, unless you were born in Africa or Asia in which case you’re likely under 35. If you are able to ask your parents the same question, the odds are much higher that they will be sporting this souvenir of the era of smallpox. What were the elements of success that enabled this scourge, which had afflicted humans for millennia, to be eradicated? This presentation will look at smallpox and other diseases, either eradicated or short-listed for eradication, and provide some historical and epidemiologic insights into this ultimate endgame of translational medicine.