The cytoplasmic replication site, huge DNA genome, and peculiar shape are the main characteristics that set the poxviruses apart. Following injection, the viral DNA merges with the bacterial DNA in a lysogenic cycle and reproduces normally with the bacterial DNA during bacterial reproduction. This chapter focuses on the biochemical components of poxvirus reproduction that have been the subject of ongoing research over the last five years, even though it is meant to be a thorough review. Replication/Reproduction The reproduction of the Variola virus begins when the virus attaches to the membrane receptors on the outside of the cell. In the lytic cycle, after the viral DNA is injected into the cell, it chops up the bacterial DNA and then directs the production of phage proteins and nucleotides from the degraded DNA which are used to make copies of the virus. Temporal regulation governs biosynthesis, and the apparent de novo production of viral membranes marks the start of an orderly developmental sequence. Type 1 topiosomerase enzymes uncoil the compressed strands of DNA and aid in replicating the early genes. ????????