

1. Looking Back in 2009 at the Dawning of Antiviral Therapy Now 50 Years Ago: An Historical Perspective	1
Erik De Clercq	
I. Introduction	3
II. Thiosemicarbazones: The First Antiviral Drugs Found Active Against the Poxvirus Vaccinia Virus	4
III. Renaissance of the Poxvirus Inhibitors: Antiviral Drugs Against a Bioterrorist Poxvirus (Variola Virus) Attack	6
IV. Benzimidazole Derivatives: Second Attempt to Launch the Antiviral Chemotherapy Era	8
V. Renaissance of the Benzimidazole Derivatives: Now Turning into Lead Candidates for the Treatment of Human CMV Infections	11
VI. 5-Substituted 2'-Deoxyuridines: Idoxuridine (IDU) and Trifluridine (TFT), the Third and Definitive Attempt to Unleash Antiviral chemotherapy	13
VII. 5-Substituted 2'-Deoxyuridines: IDU (and TFT) as the Starting Point(s) for Other 5-Substituted 2'-Deoxyuridines, that is, BVDU [(E)-5-(2-Bromovinyl)-2'-Deoxyuridine]	15
VIII. Arabinosyladenine (ara-A), Originally Conceived as an Antitumor Agent, the First Antiviral Drug Licensed and Used for Systemic treatment	16
IX. Acyclovir: The Start of the Selective Antiviral Chemotherapy Era, and Still the "Gold Standard" for HSV Therapy	18
X. Anti-influenza Virus Therapy: A First Attempt (DRB), Followed by a Second (Amantadine) and a Third Attempt (Neuraminidase Inhibitors)	20
XI. Ribavirin and Interferon, Two "Old-Timers", Joining Forces in the Treatment of a Relatively New Disease, Hepatitis C	22
XII. (S)-9-(2,3-Dihydroxypropyl)adenine (DHPA), the First Acyclic Adenosine Analog, Leading to S-Adenosylhomocysteine (SAH) Hydrolase Inhibitors as Broad-Spectrum Antiviral Agents	23
XIII. (S)-9-(2,3-Dihydroxypropyl)adenine (DHPA) Leading to the First Acyclic Nucleoside Phosphonate, (S)-9-(3-hydroxy-2-phosphonylmethoxypropyl)adenine (HPMPA), as a Broad-Spectrum Antiviral Agent	25
XIV. 9-(2-Phosphonylmethoxyethyl)adenine (PMEA), the Sister Compound of HPMPA	26
XV. From PMEA (Adefovir) to PMPA (tenofovir): It All Depends on the Substitution of a Methyl Group for a Hydrogen	28