# Otoneurological Findings in Human Immunodeficiency Virus Positive Patients

**An Essay By:**

**Anwar Moawad Mohamed El-Batawy**

(M.B., B.Ch Cairo University)

Submitted for partial fulfillment of the
M.Sc. Degree in Otolaryngology

**Supervised By:**

**Prof. Dr. Mohamed Nabil Lashin**

**Professor of Otolaryngology**

**Faculty of Medicine – Cairo University**

**Dr. Hassan Mohamed El-Hoshy**

**Assistant Professor of Otolaryngology**

**Faculty of Medicine – Cairo University**

**Dr. Badawy Chafik Khalifa**

**Lecturer of Otolaryngology**

**Faculty of Medicine – Cairo University**

**Faculty of Medicine**

**Cairo University**

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# Abstract

The human immunodeficiency virus (HIV), the causative organism of Acquired immunodeficiency syndrome (AIDS) infects and debilitates lymphocytes and macrophages leading to progressive immune compromise. This decline in immune function leaves the patient susceptible to a multiple of pathologic conditions including opportunistic infections and neoplasms. Much of this pathology can manifest in the head and neck. Thus otolaryngologists should be familiar with the disease and its multiple manifestations.

## Key words:

HIV/AIDS – Otoneurological -Facial palsy – Communication disorders - Prevention.

# List of Abbreviations

**ABR**: auditory brainstem response
**AIDS**: acquired immunodeficiency syndrome
**ART:** antiretroviral therapy
**CCR5**: chemokine receptor 5
**CDC:** The Centers for Disease Control and Prevention
**CI**: cochlear implant
**CIPRA**: Comprehensive International Program of Research on AIDS
**CMV**: Cytomegalovirus
**CXCR4**: chemokine-related receptor
**DGI:** Dynamic Gait Index
**ELISA**: enzyme-linked immune sorbent assay
**ENG:** electonystagmography
**FTA-ABS:** The fluorescent treponemal antibody absorption
**G-6-PD:** glucose-6-phosphatase dehydrogenase
**GALT:** gut-associated lymphoid tissue
**HAART:** highly active antiretroviral therapy
**HHV8:** human herpes virus 8
**HIV**: Human immunodeficiency virus
**HSV:** Herpes simplex virus
**HTLV-1**: human T-lymphotropic virus type 1
**IDUs:** Injecting Drug Users
**IgG:** immunoglobulin G
**KSHV**: Kaposi sarcoma herpes virus
**MHA-TP:** microhemagglutination-Treponema pallidum
**MTCT:** mother-to-child transmission
**NASBA:** nucleic acid sequence-based amplification
**NF-kappa-B :** nuclear factor kappa B
**NSE**: needle and syringe exchange
**OKN:** optokinetic reflex
**PCP:** *Pneumocystis* pneumonia
**PCR:** polymerase chain reaction
**PPD:** purified protein derivative
**RPR:** Rapid plasma reagent
**TMP-SMX:** trimethoprim-sulfamethoxazole
**TRECs:** T-cell receptor gene rearrangement excision circles
**VDRL** or **RPR:** Venereal Disease Research Laboratory or rapid plasmin regain
**VOR:** vestibular-ocular reflex
**VSR:** vestibulo-spinal reflex
**VVOR:** visuo-vestibular-reflex
**VZV:** varicella-zoster virus
**WHO :** World Health Organization

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# Introduction:

Acquired immunodeficiency syndrome(AIDS) is caused by Human Immunodeficiency Virus (HIV) . The illness was first described in 1981 and the virus was isolated in 1983. HIV is a retrovirus of the subfamily lentovirinae . The term retrovirus is used because the virus contains the enzyme reverse transcriptase which transcribe viral RNA to DNA, the reverse of other viral genetic transcription. HIV has selective tropism to CD4 cells(T-helper cells),which are central to the function of the human cell-mediated immune system **( Rarey,1990).**

Impairment of the human cell-mediated immunity renders the host susceptible to numerous opportunistic infections from viruses , fungi and protozoas , many of which are native to the oral cavity , pharynx and larynx . In addition to patients with typical AIDS there are others who develop AIDS-related complex consisting of generalized lymphadenopathy , fever , night sweat , fatigue , loss of weight and diarrhea which finally proceed to classically AIDS **( Janeway et al ,1999).**

Otologic complains in AIDS patients include: hearing loss (62%) , otalgia (50%) , otorrhea (31%) , vertigo (15%) and tinnitus (15%). It is not known if the neuro-otologic effects seen in AIDS is the effect of HIV alone or a combination of the effects of HIV infection coupled with opportunistic infections and/or possible toxic effects of certain therapeutic agents **( Salzer,1994).**

HIV-1 can produce severe neurological complications during the course of infection, both directly via infection of resident cells of the CNS ( resulting in a pathway of neurodegeneration ) and indirectly via the system immune suppression mechanisms and the appearance of opportunistic CNS infection **( Sandler, 1990).**

An autopsy study on 10 temporal bones from 5 HIV-positive patients refer to significant alteration of the neuroepithelium of the posterior labyrinth; less significant alteration are described in cochlea **( Chandrasekar et al,1992).**

***Spectrum of otological manifestations in HIV-+ve patients:***

***Vestibular disorders;***

In HIV-positive patients , alterations in the vestibular-ocular reflex (VOR), optokinetic reflex(OKR) and visuo-vestibular reflex(VVOR) have been documented **( Salami et al,1992).**

Instrumental studies of vestibular function and equilibrium in HIV-positive patients emphasized the early alteration of the central nervous system (CNS) rather than peripheral neuro- logical structures, often evident even in non-symptomatic patients. These findings seem to be in accordance with cerebrospinal fluid surveys **( Domenech et al,1996).**

It was suggested that vestibular screening in all HIV-positive patients is important in order to obtain more information on central nervous system function and may also be predictive of an imminent worsening of the clinical condition **( Teggi et al, 2006).**

The life expectancy of HIV-positive patients had improved over the last few years as a result of new antiretroviral strategies. This consideration justifies the clinical observation of symptoms such as dizziness. Improved diagnosis and subsequent therapeutic strategies for dizzy HIV-positive patients may help to improve their quality of life **( Teggi et al,2008).**

***Sensorineural hearing loss;***

The incidence of SNHL in patients with HIV ranges from 23 -49% , hearing loss in the high frequencies is more commonly reported than in the low frequencies **( Kohan et al,1990).**

***Infranuclear facial paralysis;***

Facial neuropathy can occur at any stage of the HIV infection. It may precede the appearance of HIV antibodies and seem to occur more frequently in healthy HIV carriers than in those with AIDS **( Mastroianni et al,1994).**

It is recommended that routine investigations of all patients with infranuclear facial paralysis should include serological testing for HIV specially in patients at risk and those with history of recent flu-like illness **( Morenikeji et al, 2009).**

***Pneumocystis carinii otitis / mastoiditis;***

Pseudomonas carinii is the most common opportunistic pathogen infecting persons with HIV infection, affecting nearly 85% patients at some point of illness. Otic Pneumocystis typically present as a unilateral polypoid mass associated with otalgia, hearing loss and otorrhea . Pneumocystis carinii otitis media and mastoiditis had been documented **( Northfelt et al,1990).**

***Kaposi's sarcoma;***

Kaposi's Sarcoma is a slowly progressive, malignant mesenchymal tumour characterized clinically by red-purple plaques and nodules that may be seen externally or internally. KS had been reported to involve the mastoid and external ear **( Linstrom et al, 1993).**

***Ramzy Hunt syndrome;***

It was reported a case of a homosexual male who was HIV +ve with Ramzy Hunt syndrome associated with facial nerve palsy **( Mishell et al,1990).**

## Aim of the study:

The aim of this study is to discuss the otoneurological findings in HIV positive patients.

Study of the disorders caused by HIV infection has allowed an improved understanding of the mechanistic behavior of viruses, specially as they are a cause of malignancies. As a result the Otolaryngologist is often called on to help control known disease processes with established treatment strategies that can directly improve quality of life.

Because many signs and symptoms of initial HIV infection present in the head and neck, the otolaryngologist/head and neck surgeon may have the opportunity and obligation to consider and to pursue this diagnosis.

# HIV Disease

Human immunodeficiency virus (HIV) disease was first described in 1981 among 2 groups—one in San Francisco and the other in New York City. Numerous young homosexual men presented with opportunistic infections that, at the time, were typically associated with severe immune deficiency due to *Pneumocystis* pneumonia (PCP) or aggressive Kaposi sarcoma. The HIV virus itself was not identified for another 2 years ; during that time, various other causes were considered, including lifestyle factors, chronic drug abuse and other infectious agents **( Ascher et al, 1993).**

HIV is a blood-borne, sexually transmissible virus. The virus is typically transmitted via sexual intercourse, shared intravenous drug paraphernalia and mother-to-child transmission (MTCT) which can occur during the birth process or during breastfeeding. The most common route of infection varies from country to country and even among cities. Co-infection with other viruses that share similar routes of transmission, such as hepatitis B, hepatitis C and human herpes virus 8 (HHV8; also known as Kaposi sarcoma herpes virus [KSHV]) is common. Two distinct species of HIV (HIV-1 and HIV-2) have been identified and each is composed of multiple subtypes or clades . All clades of HIV-1 tend to cause similar disease, but the global distribution of the clades differs. This may have implications on any future vaccine as the B clade which is predominant in the developed world (where the large pharmaceutical companies are located) is rarely found in the developing countries that are more severely affected by the disease. HIV-1 probably originated from one or more cross-species transfers from chimpanzees in central Africa **( Gao et al,1999).**

HIV-2 is closely related to viruses that infect sooty mangabeys in western Africa **( Hirsch et al,1989) .**

Genetically, HIV-1 and HIV-2 are superficially similar, but each contains unique genes and its own distinct replication process. HIV-2 carries a slightly lower risk of transmission and tends to progress more

slowly to acquired immune deficiency syndrome (AIDS) **( Popper et al, 2000).**

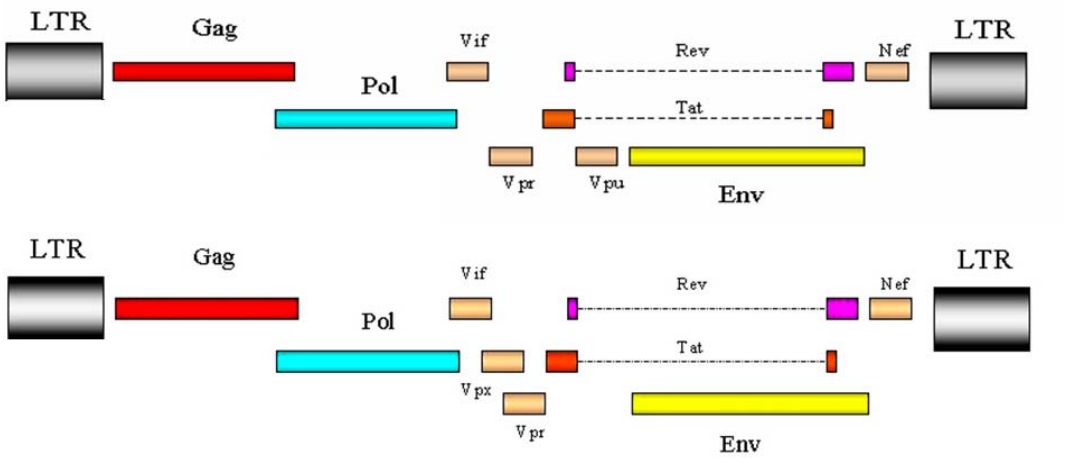
Persons infected with HIV-2 tend to have a lower viral load than people with HIV-1 and a greater viral load is associated with more rapid progression to AIDS in HIV-1 infections. HIV-2 is rare in the developed world that is why most of the research and vaccine and drug development has been (perhaps unfairly) focused on HIV-1 **( Rodríguez et al, 2006).**

A considerable amount of stigma has been attached to HIV infection, mostly because of the virus's association with sexual acquisition and the inference of sexual promiscuity. Consequences of this stigma have included discrimination and reluctance to be tested for HIV infection. However, such attitudes are inappropriate because HIV is poorly transmissible without sexual contact or blood contact and because the expected survival is long in patients with HIV infection who are receiving treatment. HIV is not transmitted during casual contact and is readily inactivated by simple detergents. Much of the concern regarding HIV infection is due to the incurability of the infection and the relentless immune decline and eventual premature death in the vast majority of infected people **( Korber et al,2000).**

## Pathophysiology:

### Virology of HIV

HIV-1 and HIV-2 are retroviruses in the Retroviridae family, *Lentivirus* genus. They are enveloped, diploid, single-stranded, positive-sense RNA viruses with a DNA intermediate which is an integrated viral genome (a provirus) that persists within the host-cell DNA. There is no fixed site of integration, but the virus tends to integrate in areas of active transcription, probably because these areas have more open chromatin and more easily accessible DNA. This greatly complicates eradication of the virus by the host as latent proviral genomes can persist without being detected by the immune system and cannot be targeted by antivirals **( Schröder et al , 2002).**




Genome layouts of HIV-1 (upper) and HIV-2 (lower)

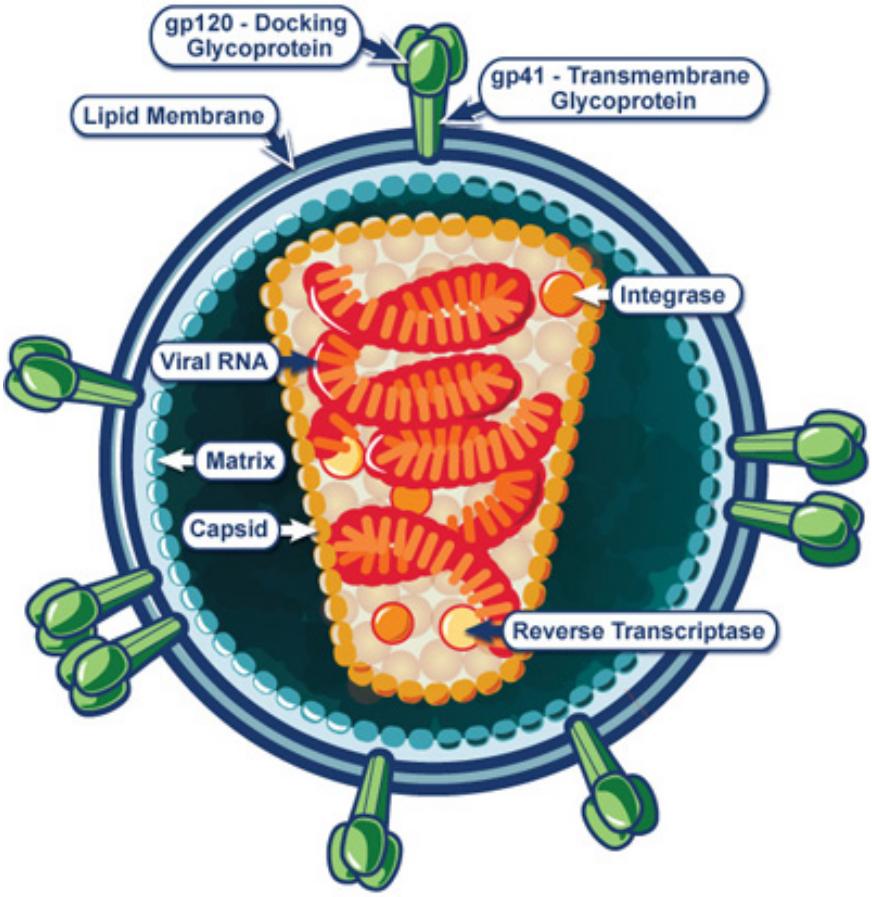
*Fig(1):Genome layouts of HIV* **( Schröder et al ,2002).**

## Steps in the HIV Replication Cycle

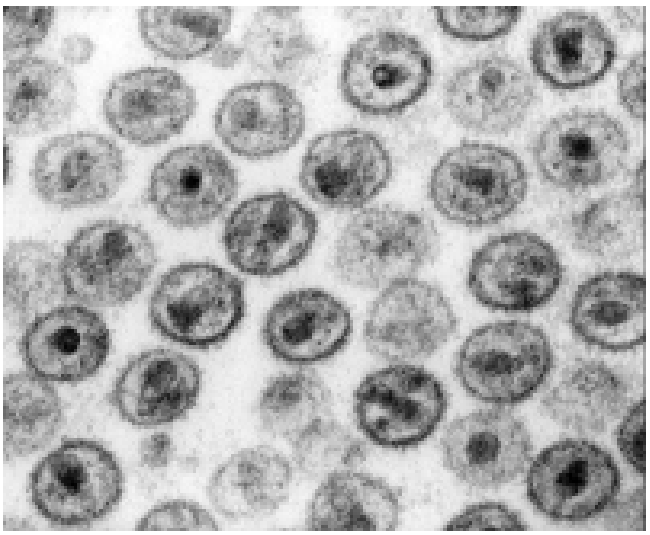
1. Fusion of the HIV cell to the host cell surface.
2. HIV RNA, reverse transcriptase, integrase and other viral proteins enter the host cell.
3. Viral DNA is formed by reverse transcription.
4. Viral DNA is transported across the nucleus and integrates into the host DNA.
5. New viral RNA is used as genomic RNA and to make viral proteins.
6. New viral RNA and proteins move to cell surface and a new, immature, HIV virus forms.
7. The virus matures by protease releasing individual HIV proteins.

**( National Institude of Allergy & Infectious Disease[NIAID],2009).**

## Structure of HIV




*Fig(2):Structure of HIV* **( Nichols,1998).**



*Fig(3):Electron microscopy of human immunodeficiency virus (HIV)–1 virion*

**( Courtesy of CDC/Dr. Edwin P. Ewing,2007).**