

THE POSITION OF AIDS IN PAKISTAN, UAE AND JORDAN

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Abstract:

AIDS is a term used for Acquired Immune-Deficiency Syndrome. It is, by definition, the end-stage disease manifestation of an infection with a called human immunodeficiency virus (HIV). The virus infects mainly two system of the body i.e. the immune system and central nervous system (CNS) and the occurrence of disease is due to the damage of these two systems. The statistics on AIDS are alarming, especially for Sub-Saharan Africa India. Some scientific studies indicated that upto one-third of all sexually active adults living in this region are already infected, up to 40% of all women and one in 10 to one in 5 children born in this region are actively infected with HIV and will be dead before having reached their fifth birthday. The information on HIV infected young adults was collected both from official and non-official sources of the following countries, Jordan, UAE, Pakistan. A big difference number of patients was found between official and non-official data. Anyhow, both data (official & non-official) are alarming due to the increase number of HIV cases. 21st century is specially dangerous to the next generation of Pakistan and Arab world because of increase in percentage of HIV cases during the last 5 years.

INTRODUCTION

In fact the AIDS virus infects mainly two systems of the body that is the immune system and central nervous system (CNS) and the occurrence of disease is due to the damage of these two systems. The scientists, academicians and medical doctors clearly differentiate between the infection with the virus (i.e. secondary infection) and the disease of AIDS. The differentiation is very simple and straight forward one and like many other viruses, HIV can infect the body and multiply in many cells inside the body without causing any ostensible damage, that is the damage of which the patient is aware. In this respect HIV is not unique. The herpes viruses also do this (Schoub, 1994).

The electronic and press media have often in a very dramatic way present the anxieties and the fears of the "person in the street" as well as given prematurely false hopes about drugs and vaccine "break through".

Statistics on AIDS are often dangerous, some time they would suggest a disease of serious, yes, but not critical. For example cumulative number of AIDS cases reported to WHO as of 2 July 1993 was 718,894 and even the WHO estimate one

million cases of AIDS is still overshadowed by the annual death toll of two to three million each for measles and tuberculosis.

At other times statistics on AIDS are alarming, especially those coming from Sub-Saharan Africa where less than 10% of the world's population are responsible for some 60% of all HIV infections. Furthermore, that one-fortieth of all adults in this part of the world are infected with a terminal disease and each of these individuals can, in turn, act as a fountain of infection for yet further spread, clearly indicates an epidemic of towering proportions. Some scientific studies indicate that upto one-third of all sexually active adults living in region of Sub-Saharan Africa are already infected, 40% of all women attending antenatal clinics in certain urban centers are HIV positive and therefore that about one in 10 to one to 5 children born in this part of the world will be actively infected with the virus and will be dead before having reached their fifth birthday. The WHO has estimated that about one million children globally have been infected, over half of them have developed AIDS or have died (Schoub, 1994).

In most countries of the Continent Africa AIDS is the leading cause of adult death and in some studies, for example women of child-bearing age in Rwanda, HIV disease was responsible for 90% of deaths (WHO report of 1993; Schoub 1994).

In USA the average cost of treating an AIDS patient has been estimated to be \$ 27950 to \$ 40455, which is the total federal bill for HIV in 1992 has been estimated to be \$ 4.3 billion. The cost of treating an AIDS patient in Africa has been estimated to be \$ 150- \$ 400 compared with an average per capita expenditure on health of \$ 15 (Soboub, 1994; Macilwain, 1996; Cohen, 1996).

MODE OF ACTION & TRANSMISSION OF AIDS VIRUS:

It can be transmitted by three ways i) through sexual intercourse ii) sharing unsterilized needles and syringes, blood transfusion, organ donation for transplantation iii) by infected women to their offspring by 3 possible mechanism a) to foetus through maternal circulation b) to infant during labour and delivery c) after birth through infected milk (Schoub, 1994).

The mechanism of invasion of AIDS virus to immune system is totally related to the destruction of T4-cells. What are T4-cells? For that the knowledge about immune system is necessary and that can be obtained from any Immunology text book. AIDS virus is known to kill normal cells by replication, budding and damaging the cell membrane. HIV might also kills T4-cells indirectly by means of a viral protein gp

120, that is displayed on an infected cell's surface. Molecule on T4-cells "Cat receptor" has strong affinity for gp 120, therefore, healthy T4-cells can bind to the gp 120 & merge with infected cells. The end result, called syncytium, for T4-cell is death. Therefore, once it enters into the healthy cells, both healthy and infected cells, are destroyed easily. HIV also elicits normal cellular immune defense against infected cells. With or without the help of antibodies, cytotoxic cells can destroy an infected cell which displays viral proteins on its surface. Finally free gp 120 may circulate in the blood of people with HIV. Free protein may bind to CD₄ receptor of uninfected cells, making them & appear or infected and evoking an immune response (Schoub, 1994; Levine et al, 1996).

Sign and Symptoms of an infected person includes (Schoub, 1994):

- Sweating, excessive night sweats.
- Sore throat, coughing, shortness of breath, constipation.
- Skin rashes or lesions, weight loss, headache, memory loss.
- Anxiety, stress, genital sores, diplopia, chest pain.
- Back pain, muscles pain, bone pain or tenderness, seizures.

Diagnostic test for AIDS (Schoub, 1994):

Presence of one of these disorders is first sign of AIDS in patient that is :

- HIV antibody test i.e. ELISA (Enzyme Linked Immunoabsorbent Assay), if positive.
- Absolute CD4 lymphocyte count is <200.
- P24 antigen is abnormal.
- T (Thymus derived) lymphocyte count is abnormal.

THERAPY (Abrams, 1990; De Clercq 1991):

The drugs which are used in the cure or therapy of this are categorized according to their mode of action such as.

- i) Attachment steps in early stages of HIV replication (Schoub, 1994 Brown, 1992; Richman, 1996):

In early stages of HIV replication (Fig. 1):

- i) Attachment steps in early stage of HIV replication
- ii) Reverse transcriptase in early stages of HIV replication

Soluble CD4 OR Anti CD4 OR rCD4 Drugs.

Mode of action: Inhibit viral binding to CD4 receptor.

Comments:

- A Genetically engineered of CD₄. Phase I trial under way.
- B Soluble CD₄ is unstable in the body
It is too rapidly inactive for it to be clinically useful.
To render it more stable CD₄ may be fused to immunoglobuline. The CD₄ immunoglobulins complex is referred to as an immunoadhesin.

- ii) Reverse transcriptase in early stages of HIV replication (Schoub, 1994, Meyaard et al. 1992; Cohen, 1996):

AZT (AIDS ZODPVIDOME THERAPY)

Mode of action: Reverse transcriptase inhibitor, chain terminator.

Comments:

- A Clinical trials with AZT indicate that the drug significantly reduces mortality in patient with ARC (AIDS Related Complex) or with AIDS of recent onset.
- B Patient has fewer opportunistic infection and has increase T4-lymphocyte counts while on therapy.

Adverse effects:

Anemia, neutropenia, nausea, headache, and / or ashes

Drug interaction (Schoub 1994; Cohen, 1996):

- A Probenecide shows the metabolism and excretion of AZT, increase the risk of hematotoxicity.
- B Acetaminophen: interferon with glucuronidation of AZT in the live.

AZT Failure: is caused by virus becoming resistant to drug, or drug ceasing to be effective in patient even through the virus remains sensitive when tested in Laboratory, so called "refractoriness" or because drug has to be withdrawn because of development or prohibitive toxicity. The drug of choice to treat anemia with AZT is "Erythropoietin".

DDI and DDC (Dideoxyionsine & Dideoxycytidine) (Schoub, 1994):

Mode of action: Reverse transcriptase inhibitor, chain terminator.

Comments: For DIM: Relatively little bone marrow toxicity in vitro. Phase I trials under way.

For DDC: Antiviral effects are even at very low dose, toxic effects on peripheral nerves can be reduced by taking alternatively with AZT. Phase II trials under way;

both alone and in combination with AZT.

Note: But in 1994, there is a research for this point & they make a combination between AZT, DDI & DDC.

Late Stage of HIV Replication (Fig.2):

- i) Transcription steps in late stage of HIV.
- ii) Transcription steps in late stage of HIV.
- iii) Proteolysis steps in late stage of HIV.
- iv) Glycosylation steps in late stage of HIV.
- v) Myristylation steps in late stage of HIV.

i) Transcription Steps:

TIBO (Tetrahydroimidazo[4,5,7k]-benodiazepin-2(IH)-one & thione) derivations which are related to benzodiazepines, mode of action has not been definitively established. At present, the limited supply has hampered more extensive investigation of these agents:

ii) Translation Steps:

Trichosanthin, a natural product obtained from Chinese cucumber, *Trichosanthes kirilowii* inhibits the viral protein synthesis at the level of ribosomal activity, which is presently under investigation.

iii) Proteolysis Steps:

Enzyme protease, which is responsible for splitting of precursor protein molecules into their smaller functional component proteins. It appears to be the exciting & promising target on which the future drug development is based. Substance directly inhibits the enzyme and specific peptide molecules which are analogues of natural peptide fragments, are designed to inactivate enzyme on the same principle as that by which the dideoxynucleoside analogues inactivate reverse transcriptase.

iv) Glycosylation Steps:

The most important compounds for these step is castanospermin, obtained from Australian chestnut, *Castanospemeum australe* as an antibiotic called Deoxynojirimycin.

v) Myristylation Steps:

It is investigated as a possible target for antiviral drug development and as a number of myristic acid analogues are currently under evaluation.

IMMUNE MODULAR THERAPY (Schoub, 1994; Mill & Littman, 1996):

Increase in the activity of three possible interferon can enhance the activity of immune against HIV, such as :

- 1) Interleukin-2
- 2) Alpha & gamma interferon
- 3) AZT plus alpha interferon.

FINALLY

The linkage of CD4 molecule to a toxic material such as exotoxin from an organism called *Pseudomonae* produce a hybrid molecule called CD-PE40 (PE=Pseudomonas Exotoxin). So when CD₄ component attaches itself to gp 120 it release its lethal cargo with the cell, there it destroys only the infected cells.

Ricin from castorbean also couples out targeting vehicles. It is one of the most lethal biological compounds.

INFECTIONS WHICH ARE COMMONLY ASSOCIATED WITH AIDS DISEASE (SCHOUB, 1994):**1) Protozoal infection:**

- a) PCP (Pneumocystis carinii pneumonia) drug of choice
 - i) Co-trimoxazol
 - ii) Pentamidine
- b) Toxoplasmosis (*Toxoplasma gondii*) drug of choice
 - i) Combination of pyrimethamine & sulphadiazine.

2) Bacterial infection:

- T.R. (*Mycobacterium tuberculosis*) drug of choice
- i) Rifabutin
 - iii) Ciprofloxacin

3) Fungal infection:

- i) Candidiasis
 - a) Oropharyngeal - Topical Nystatin - Topical Amphotericin
 - b) Oesophagitis - ketoconazole - fluconazole & Itraconazole
- ii) Cryptococcosis (*Cryptococcus neoformans*) - amphotericin i.v. - fluconazole.

4) Viral infection:

- i) Cytomegalovirus (CMV)
 - cancioclovir
 - fluconazole
- ii) Helper simplex/Herpes Zoster (HSV) - acyclovv.

5) Cancer:

- AIDS-related kaposis sarcoma (KS)
- Vincristine 2 mg + Neomycin 30mg
- A combination of AZT & a-interferousa.

THE GLOBAL STATUS OF AIDS AND PRESENT SITUATION IN PAKISTAN, UAE & JORDAN:

The cumulative number of aids cases reported throughout the world is published bi-annually in a publication of the WHO called the "Weekly Epidemiological Record". In its publication of 2 July 1993 the total number of cases reported cumulatively in the world upto that date was 718, 894, of which some 51.6% (371,086) were reported from the America, 34.4% (247, 577) from Africa, 12.9% (92,482) from Euope, 0.6% (4188) from oceania and 0.5% (3561) from Asia.

The following table shows the present position of AIDS in Pakistan, Jordan, UAE and India.

	Pakistan		Jordan		UAE		India	
	Off.	non-off.	Off.	non-off.	Off.	non-off.	Off.	non-off.
Male	46	50791	38	1500	8	1000	3 m	above 3 m
Female	ND	1000	ND	100	ND	100	ND	-
Children	ND	30	ND	4	ND	16	80,000	100,000
Total	46*	51821	38*	1604	8*	1116	3.08 m	3.1 m

Off. = Official, non-off. = non-official, ND = Not Declared, m = million

* WHO report of EMR 1 Jan. - 31 Dec. 1994, printed in March 1995.

According to daily DAWN newspaper dated 19 July 1996, 22 million people have been infected world over by AIDS and one seventh of it are present in India. In another report the same newspaper, August 1996, indicated the presence of at least 80,000 HIV positive children in India and the cause of their disease are their infected parents. It has also been reported that the increase rate of infection in India is 10 times more than Europe and America and is due to subtype virus "C" and women make up 40% of the victims by their husbands.

Daily DAWN 24 July 1996 reported that in province of Sindh of Pakistan at least 370 patients have been found HIV positive. In Daily Jang (a newspaper), 25th October, 1996, Pakistan Council of Research for AIDS has reported a figure of 50,000 AIDS patients in Pakistan. But non-official reports indicates that the number of cases all over Pakistan are much higher than official one and the same thing was also found in the official data of UAE and Jordan.

There are two basic reasons behind the hiding of AIDS data:

- i) Pakistan, UAE and Jordan are Muslim states and according to Muslim religion a person can not have sexual contact with any illegal person (legal persons are wife and husband). An illegal contact has punishment, therefore, most of the time, due to fear of punishment and society, infected people do not like to report concerned authorities whether they received it by other means (i.e. by blood transfusion, needles or by organ transplantation etc.).
- ii) Government of these states are hiding the cases due to several reasons:
 - a) chances of inharasment and law & order situation
 - b) hateness of common people to rich people who are supposed to be responsible for the spread of disease (a concept of common people).
 - c) fear of loss in tourists' income
 - d) loss of labours and economics
 - e) another reason is weak drug control system especially in Pakistan.

According to WHO annual report of Mediteranean Region, I January-31 December 1994, showed a very low number of AIDS cases in Pakistan (46), Jordan (38) and UAE (8) but non-official sources indicated at least 10 times more cases during the same year.

But whatever the numbers reported by official and non-official sources the most important and alarming thing is the increase rate of disease incident per year. Increase in number of victims in India are quite dangerous to Pakistan, Jordan, UAE and Saudia Arabia and other Gulf countries, because of large population of Indians

in these countries and bilateral relationship in education and joint -ventures. This needs a carefull protection on large scale, screening & testing of suspected person, awareness and precautionary measurement about the disease.

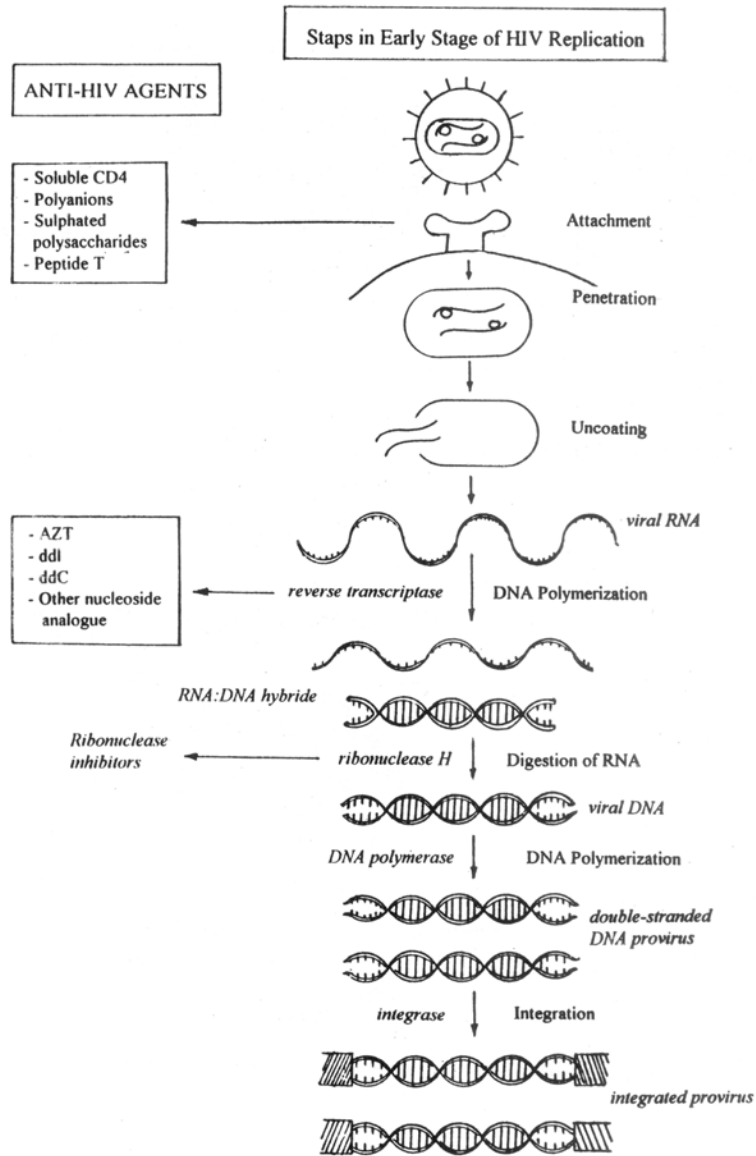


Fig. 1: Steps in early stage of HIV replication showing sites of activity of anti HIV drugs.

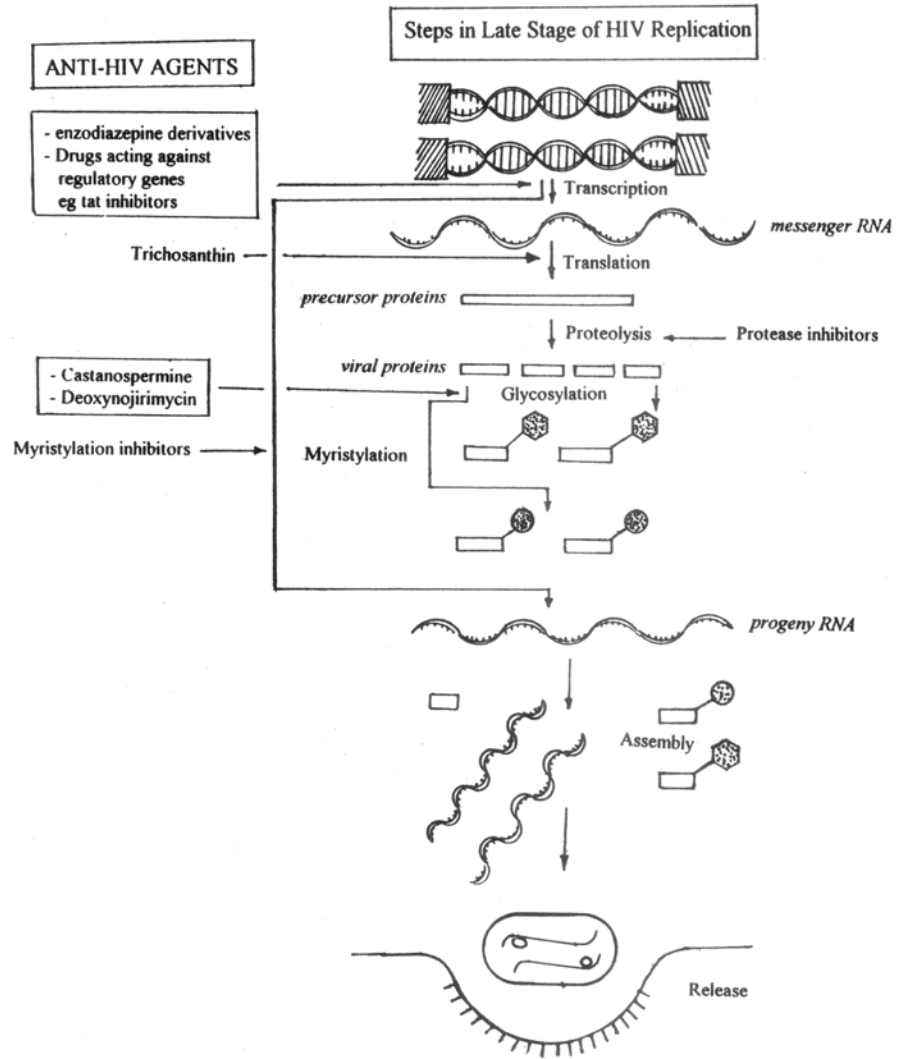


Fig. 2: Steps in late stage of HIV replication showing sites of activity of anti HIV drugs.

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