*Krzysztof Simon, Robert Simon, Sylwia Serafińska*

# HIV/AIDS AND AGING

## ZAKAŻENIE HIV/AIDS A PROCES STARZENIA SIĘ

Department of Infectious Diseases, Hepatology and Acquired Immune Deficiencies,
Wrocław University of Medicine, Poland

STRESZCZENIE

W drugiej połowie XX wieku średnia wieku życia człowieka, szczególnie w krajach uprzemysłowionych, znacznie się wydłużyła, a problemy zdrowotne ludzi w wieku podeszłym stały się dużym problemem społecznym i klinicznym.

W porównaniu z ludźmi młodymi, problemy zdrowotne u osób w starszym wieku występują częściej i mają cięższy przebieg. Dotyczy to zwłaszcza chorób o etiologii zakaźnej, które cechuje gorsze rokowanie i często odmienny nietypowy obraz kliniczny. Również wyniki badań obrazowych jak i wyniki badań laboratoryjnych u osób w starszym wieku bywają nietypowe i odmienne . Różnice dotyczą też epidemiologii zakażeń jak i stosowanych metod leczenia.

Do najważniejszych przyczyn zaliczamy: postępujące w miarę upływu lat starzenie się układu immunologicznego, niedożywienie, narastająca liczba związanych z wiekiem problemów natury socjalnej, psychologicznej oraz ekonomicznej, jak i zmian fizjologicznych czy anatomicznych. Pacjenci zakażeni HIV w starszym wieku, w porównaniu z osobami młodszymi, w momencie rozpoznania zakażenia charakteryzują się niższą liczbą limfocytów o fenotypie CD4, wykazują szybszą progresję choroby, mają więcej zakażeń oportunistycznych i krótszy okres przeżycia - i to niezależnie, kiedy u nich rozpoznano zakażenie HIV.

**Słowa kluczowe***: zakażenie HIV/AIDS, starzenie się, zakażenia oportunistyczne, leczenie antyretrowirusowe*

ABSTRACT

Average life expectancy in developed countries has rapidly increased in the middle of the 20th century and the geriatric problems have become an increasingly important issue. Many diseases in the elderly are more frequent and more severe in comparison to the younger population. This is certainly true for the infectious diseases which are in the elderly associated with poor outcome, moreover they have often the distinct features with respect to clinical presentation, laboratory and imaging test results, microbial epidemiology, and methods of treatment. The most important reasons why the diseases in the elderly are more frequent and more severe these are: typical for advanced age immunosenescence, malnutrition, large number of age-associated social, psychological, economical, moreover physiological and anatomical alterations. The older HIV positive adults, have lower CD4 counts at moment of diagnosis, faster progression to AIDS, more opportunistic infections, shorter survival rate than younger adults - regardless of when they were first diagnosed with HIV.

**Key words:** *HIV/AIDS infection, aging, opportunistic infections, antiretroviral therapy*

## INTRODUCTION

The average life expectancy in the developed countries has rapidly increased in the second half of the 20th century and the geriatric problems have become an increasingly important issue. For example in Switzerland- in 1990 the 2% of population was between 65-79 years and 0,5% above >80y, but one hundred years later in 2000 they had 11,4% population between 65-75 years, and 4% >80 years .The epidemiologists suppose that in 2060 15% of the total population will be between 65-75 years and 9% >80 years (altogether 24% of population). Probably the same situation is going to happen in USA and in other developed countries. Till now there are differences in definition ”elderly people”. At the beginning of the XX century all people above 50 years old were assessed as older people. Up to now this is probably true for many poor countries. At present all people above 75 years old are considered to be elderly. In comparison with the younger population

the many diseases in the elderly are more frequent and more severe. This is certainly true for infectious diseases which are in the elderly moreover associated with poor outcome, very often they have the distinct features with respect to clinical presentation, laboratory and imaging test results, microbial epidemiology, and the methods of treatment. Another important problem among older people it is the infection control. The most important reasons why the diseases in the elderly are more frequent and more severe these are: typical for advanced age immunosenescence, malnutrition,the large number of age-associated social, psychological, physiological and anatomical alterations and some epidemiological elements(1,2,3).

## HIV/AIDS - EPIDEMIOLOGY

The problem of HIV and AIDS infection appeared as the definite medical problem in 1981, at first as the important health problem in white young men with homosexual behavior. As they were getting older then quickly developed immunity impairment and occurrence of clinically evident AIDS. (4-7). In the most of HIV positive patients the chance of being aged were very low still 20 years ago. Now in the era of the high active antiretroviral therapy(HAART) the life expectancy of HIV-infected patients has dramatically improved so the essential change of age profile of HIV patients, but also the mode of HIV transmission, has been observed. Currently in many countries the predominant mode of HIV is sexual ( mostly heterosexual) and vertical transmission ( except Eastern European countries and Southeast China where IDUs are the principal at risk). It is interesting that heterosexual transmission of HIV is independent on a patient's age. The number of persons at age over 50 and older ones with HIV/AIDS is growing instantly, especially in the developed countries (8,9,10), in Poland too (our own observations). For example, over 61% patients at age over 50, in area of New York have been HIV positive for last 5 years. According other data from USA area, in 2005 the patients at age over 50 made 15% of all new discovered cases with HIV /AIDS, 24 % of all patients living with HIV/AIDS (in 2001 about. 17%), 19% new diagnosed cases with clinically evident AIDS and up to 29% patients living with AIDS. Simultaneously the patients at age over 50 made up to 35% of all the dead due to AIDS in USA. However the essential ethnic differences has been observed. HIV infection is diagnosed over 12x more frequently among Afro-Americans (51,7/100 000) and 5x more frequently among Latinos (21,4/100000) in comparison with Caucasian race (4,2/100 000) (11-16).

## CAUSES OF HIV/AIDS INFECTION GROWTH IN PERSONS AT AGE OVER 50 AND OLDER ONES

Undoubtedly it is the complex and interesting problem, very heterogeneous in different countries. It depends as well on the wealth index of these societies i.e. among other things, on the access to the health service and possibilities of HIV/AIDS treatment, as on the culture or religious tradition.

The elementary and first reason for increase of a number of patients at age over 50 with HIV/AIDS **is the development and increase the access to the modern antiretroviral therapy, as well to the better methods and therapeutic management of infectious diseases and the neoplasm defining AIDS**.

Looking into the past, in the period 1982-1985 we were completely helpless and with no hope for effective restraining the disease development, the years 1988-1996 were characterized by the progressive although slow growth, as far as the possibilities of the antiretroviral therapy, defined as the high active antiretroviral therapy (HAART).This therapy turned out to be effective enough to make some clinicians so optimistic (years 1996-1999), that they demonstrated the thesis about changing HIV infection from the fast development of the immunodeficiency into the disease with radically chronic character.

Undoubtedly, it takes a place in many cases, however we have still inquired: how long we are able to control HIV viremia effectively, in context of the observed drug resistance increase together with the antiretroviral therapy being prolonged and as well the prolonged lives of these patients.

As neither of presently used drugs nor drug combination is virucidal, just only virostatic it means that so far we have not had at our command some possibilities of the permanent eradication of HIV (8,10,13,16).

Moreover other important causes of the growth of HIV infection number in patients at age over 50 should be also taken into consideration:

- **it is groundless point of view, demonstrated also in the medical background, that the risk of HIV infection refers only to young people with risky sexual behavior or to the drug addicts;**
- **the lack of the elementary education in this field,**
- **the lack of awareness of the risk factors for getting HIV;**
- **unprotected heterosexual or homosexual intercourse.**

The last problem especially refers to women at postmenopausal age, who needn't use contraception so they rarely demand from their new met partners making safe sex, using condoms or presenting the current results

or making tests on probable HIV infection. As well the dryness of mucocolpos, which is typically more frequently present at this age, is conducive the transmission of venereal diseases and facilitates HIV infection.

Also other essential causes of HIV infection transmission in patients of this age group, which should be numbered , these are the frequent changes of family situation(**divorce, death of partner),**that facilitates the negligence of the elementary safety rules during meeting a new partner .

The patients at the mature age make examinations for HIV definitely rare than younger people, because of the mentioned above causes as well due to groundless shame and fear of rejection by family (14,15,16).

**Finally, many mistakes in this field are made by the health service.** The most of doctors, especially general practitioners underestimate the possibility and risk of getting HIV infection by the patients at age over 50 and older ones, so these examination are more seldom commissioned by doctors. The doctors inquire these patients more unusually about their sexual behavior and taking narcotics, also in the past, as well the patients avoid or refuse to talk about it. The reported pathologic syndromes and deviations from the standards noticed during the physical examinations, often even typical for the progressive immunodeficiency and AIDS, are thought as the diseases typical for the mature or old age of the patients, especially it refers to the deterioration of mental and physical ability, the progressive asthenia and fatigability, the recurring various infections, the weight decrease. It often delays the early diagnosis, so essential for life of HIV positive patient, and in this way it delays turning on the antiretroviral therapy, early enough to protect before the deep and irreversible damage of the immunological system (1,8,9,15,16).

The attitudes and opinions on the possibilities of HIV infections in the patients at mature or old age were estimated in the sociological studies made especially in USA area. The received estimations were very depressing. As the most of people of inquire, especially the younger ones thought:

- that the patients at elder age are not interested in sexual life and even they are, they make it only in the context of the heterosexual monogamous relationships;
- even these persons are interested in sex, there are not many persons, who wanted to make sexual intercourses with them;
- the persons using narcotics are not essentially met in this group, even though they had used narcotics, it was many years ago.

If we take into consideration such social opinions and attitudes, it will be hard to expect the inhibition of the urgent growth of HIV/AIDS infections and incidence in this age group. Moreover, the current epidemiological data confirmed that drug use accounts for more than 16% of infections of people over 50 (9,15-19).

## THE AGING AND IMMUNE SYSTEM

It is thought, that the aging defined as the gradual, progressive together with the lapse of time, detoriation of function of the most of systems and organs, it starts only after the thirtieth year of life. During the lapse of time it reaches to the gradual impairment of ARID-age realeted immune deficiency, as well the pharmacokinetics and the final result of the influence of many drugs. This process is named the usual aging, unless the coexisting diseases occur. It is opposite to the pathologic aging being the result of coexisiting diseases with various aetiology.

We meet all this situations in the mature or elderly patients. From this point of view, the HIV infection overlaps the slowly progressive within the lapse of time, dysfunction of different organs and essentially shallow physiological immune deficiency, and mainly specific immunity. The unspecific response is usually less afflicted by the organism aging process.

The HIV infection causes not only the progressive decrease of the number and function of lymphocytes with CD4 phenotype (fundamental for functioning of the immunologic system); it is also the chronic inflammation coming to the immune activation and complications of chronic inflammation. In elderly HIV infected patients has been observed premature senescence of T-cells and vascular endothelial cells altogether. Moreover in people in older age who had good immune reconstitiution (CD4 counts had gone up, low HIV viral load) in consequence of successful cART , their T-cell populations were consistent with those of people more than 32 years older (1,2,4-8).

## THE TYPICAL CLINICAL PROBLEMS CONNECTED WITH HIV/AIDS INFECTION IN PERSONS AT AGE OVER 50 AND ELDER ONES

Certainly the diseases defining AIDS in these age groups are identical as in the younger patients (8,9,16,18). However, there is faster HIV disease progression and more non-AIDS defining condition with older age. Especially **infections** occur more frequently and their course is more serious , worse prognosis as well often the untypical clinical picture. The essential reason for it is the progressive aging of the immunological system, often coexisting malnutrition as well the numerous problems of economical, psychological and social nature. Moreover the diseases defining AIDS

overlap on the chronic diseases typically connected with the progressive age of patients.

It has an effect on the problems in diagnosis as well in the effective and safe management. These are the most frequently observed diseases with infectious etiology, present in these age groups: the infection, the most frequently interstitial pneumonia, caused by *Pneumocystis jirovecii (earlier P.carinii),* the zoster-often generalized, tuberculosis, CMV infection, as well candidiasis of mucosa of the alimentary and respiratory tracts, especially of an oral cavity (oral trush) and an esophagus.

As well Kaposi sarcoma, etiologically connected with the HHV-8 (KSV-8) herpes virus infection, is observed essentially more frequent in the HIV positive patients in the older age groups, especially often, although not exceptionally in the men with homosexual or bisexual behaviors.

On the other hand, the essential infection problems in HIV positive women are diseases transmitted by heterosexual contacts.

Typical for the post menopause period changes in the vaginal mucous membrane is conducive to spread any diseases transmitted by a sexual tract. In comparison with the female patients, being in the same age groups but HIV negative, the infections by anascogenic yeasts (recurring and weakly susceptible to therapy) is observed more frequently as well the infections by various strains of human papilloma virus, that enlarges the risk of appearance of carcinoma and condylomas, in this group the inflammatory diseases of pelvis also occur more often (15,16,18).

The appearing infections overlap the essential and more often observed in the older HIV positive patients, than in younger patients, the organic and functional pathologies of nervous system, as well the problems of psychological nature.

The HIV positive patients are more often stricken with the dementia syndromes connected with infection of Central Nervous System (CNS) by very HIV (although usually the coexisting infection of CNS by cytomegalic virus CMV is recorded). HIV dementia in this group of patients has the violent beginning and demonstrates the fast progression that makes the patient unable for the independent existence. Unfortunately, as far as these patients are concerned, the dementia syndromes connected with HIV are diagnosed either as Alzheimer disease (although aphasia isn't observed in dementia) or Parkinson disease (however, bradykinesa does not occur).

The functional disorders of CNS, usually as depression and abusing psychotropic drugs are observed much more frequently in the HIV positive persons than in the not infected ones located in the same age groups (8,12,18,20,21).

## OTHER CLINICAL PROBLEMS, INDIRECTLY CONNECTED HIV/ AIDS INFECTION OR THE MANAGED ANTIRETROVIRAL THERAPY IN PERSONS AT AGE OVER 50 AND ELDER ONES

It was demonstrated that up to 60% of HIV positive patients at age over 60 has got hypertension to a various degree, as well the lipid balance disorders. It is often connected with the premature and advanced atherosclerosis, including myocardial ischemia. Still at the beginning of XX century it was demonstrated, that the chronic inflammatory states and infections including the lipid balance disorders determine the essential factor of atherosclerosis development, definitely more essential than each of these factors separately (20,21). It was observed that the series of the antiretroviral drugs used in the combined therapy of HIV infections (cART, HAART), also causes the extensive adipose balance e.g. some protease inhibitors , that precludes use of them in this HIV positive age group, either if use of them is impossible to avoid the progress of atherosclerosis including all its consequences (10,22-25).

The next essential problem is, as they are getting older, the increasing incidence of neoplasms. The rates of fatal non-AIDS –defining neoplasms is more than 5 times higher than rates for AIDS-defining malignancies among older HIV-infected above 65 and increases with age after 50; especially the lung cancer, the colorectal or prostate cancer (9,10,12,16,24). E.g. the incidence of the colon cancer in the patients at age 40-50 years is estimated as 15/10000 per year but in the patients over 80 years old it is 400/100000/ per year. Certainly these problems overlapping on HIV/AIDS infection, on the one hand hamper and even sometimes prevent the antiretroviral therapy procedure and on the other hand the radical , often complex therapeutic procedure.

Another essential clinical problem that refers the most frequently but not only the Caucasian race women living in the Northern hemisphere it is increasing as the years went, reduction in the bone mass i.e. osteoporosis. However it has been known for ages that the very HIV infection as the years of the infection duration went, affects the progressive bone mass defect, which intensifies also after some antiretroviral drugs i.e. the nucleoside analogues (9,24,25).

## THE POSSIBILITIES AND SAFETY OF HIV/AIDS INFECTION TREATMENT IN PATIENTS AT AGE OVER 50.

At the moment of diagnosis HIV/AIDS infection in the patients at age over 50 it is demonstrates usually the

lower values of lymphocytes with CD4 phenotype and the faster progression of the infection,the higher number of the overlapping each other infections, including of course the opportunistic ones as well other diseases defining AIDS. Certainly the risk of progression increases altogether with the lapse of the patients age. However the differences between these patients and HIV positive younger population ,when it comes to the viremia reduction after turning on the antiretroviral therapy (HAART) were not demonstrated while the essential differences (to the older patients disadvantage), when it comes to the improvement of the immunological system activity, expected as the consequence of effective inhibition of HIV replication were demonstrated. The possibilities and efficiencies of managing the effective antiretroviral therapy are certainly limited by the mentioned above clinical problems (25,26,27). The changes caused by aging can resemble or worsen HAART side effects.

Basing on the clinical experience which has been obtained as well on the possibilities of the currently accessible antiviral therapy, it was made the statistical simulation of survival chances of the HIV positive infected patients in different age groups, at whom were assumed the hypothetical number of CD4 lymphocytes at the moment of diagnosis as 500kom/mm3 and HIV viraemia (virus charge) at the level 10 thousands of copies/mm2. It was demonstrated that the chance of survival in a patient at age of 30 years would be next 26.8 years, at age of 40 years- 24.4 years and when it comes to a person at age 50 years it would be 14.6 years. It is interesting that the risk of death due to diseases different from HIV calculated during the observation period was in the patients at age 30 years would be 36% at 40 years old persons for 53% and in 50 years old person for 72%. These calculations show that the most of HIV infected patients will die due to causes different from the progressive immunodeficiency (28).

## REFERENCES


1. Gavazzi G, Krause KH. Ageing and infection. Lancet. Infect Dis 2002;2:659-666.
2. Havlik R J, Kaminski DM. Aging before your time. The Body, fall 2009, www. thebody. com/content/ whatis/ art.54795.html,1-5.
3. Międzynarodowa Strategia Działania w Kwestii Starzenia się Społeczeństw.(2002 r.), www. unic .un.org.pl/ ageing/wstep.php
4. Castle SC. Clinical relevance of age-related immune dysfunction. Clin Infect Dis 2000; 31: 576-85.
5. Herman WA, Łącka K. Proces starzenia a układ immunologiczny. Pol Arch Med Wewn 2004;112 (6):1487-1495.
6. Wieczorkowska-Tobis K. Zmiany narządowe w procesie starzenia. Pol Arch Med Wewn 2008;118(suppl):63-69.
7. Jabłecka A ,Korzeniowska K, Smolarek I. Farmakokinetyka leków w wieku podeszłym. Pol Arch Med Wewn 2008;118 (suppl):43-46.
8. Schmid GP, Williams BG, Garcia-Caleja JM, et al. The unexplored story of HIV and ageing . Bull WHO 2009;87(3):161-244.
9. HIV/AIDS among persons aged 50 and older.The Body, February 2008,www. thebody. com/content/ whatis/ art46524.html,?ts=pf,1-3.
10. Older people and HIV, May 2009,fact Sheet No.616. www.aidsinfonet.org
11. Hall H I, Song R, Rhodes P, et al. Estimation of HIV incidence in the United States. JAMA 2008;300:520-529.
12. Rodriguez S ,Alvarez MR. Normal aging and AIDS. Arch Gerontol Geriatr 2003;36:57-65.
13. Coleman C L. Transmission of HIV infection among older adults: a population at risk J Assoc Nurses in AIDS Care 2003:82-85.
14. Lindau ST, Schumm MA, Laumann EO, et al. A study of sexuality and health among older adults in the United States. N Eng J Med 2007;357:762–774.
15. Lindau ST , Leitsch SA, Lundberg KL, Jerome J. Older women's attitudes, behavior, and communication about sex and HIV: a community-based study. J Womens Health 2006;6:747–753.
16. Karpiak S. Reality demands change;people over age 50 living with HIV continues to increase The Body, April-June 2007,www. thebody. com/content/ whatis/ art44596. html,1-3
17. Szczuka I. Grużlica w Polsce w 2007 roku. Przegl Epidemiol 2009;63(2):281-286.
18. Linley L, Hall HI, An Q, et al. HIV/AIDS diagnoses among persons fifty years and older in 33 states, 2001–2005. National HIV Prevention Conference, December 2007; Atlanta. Abstract B08-1.
19. Staszewska E, Laskus I,Rosińska M. Zakażenia HIV i zachorowania na AIDS w Polsce w 2007 roku. Przegl Epidemiol 2009;63(2):271-278.
20. Pinto AN. AIDS/HIV infection and cerebrovascular disease Semin.Cerebrovasc. Dis. Stroke, 2005; 5:40-46.
21. Hinkin CH ,Castellon SA, Atkinson J H,Goodkin K. Neuropsychiatric aspects of HIV infection among older adults. J Clin Epidemiol 2001;54:S44-S52.
22. Fabricant C G, Fabricant J, Litrenta MM, Minick CR. Virus-induced atherosclerosis. J Exp Med 1978;148:335-340.
23. Libby P. Inflammation in atherosclerosis. Nature 2002;420:868-874.
24. Engels E. Human immunodeficiency virus infection,aging and cancer .J Clin Epidemiol 2001 ;54: S29-S34.
25. Tumbarello M,Rabagliati T,de Gaetano Donati K, et al. Older HIV-positive patients in the era of highly active antiretroviral therapy:changing of a scenario. AIDS 2003;17:128-31.
26. Stuart J C,Hamman D,Borleffs J, et al. Reconstitiution of naïve T-cells during antiretroviral treatment of HIV-infected adults is dependent on age. AIDS 2002;16:2263-2266.
27. Stricker J D. Over 50 with HIV. ACRIA Update, 2004;13,3,1.

28. Braithwaite RS, Justice AC, Chung-Chou H.Chang, et al.Estimating the proportion of patients infected with HIV who will die of comorbid diseases. Am J Med 2005;118:890-898.

Received: 17.03.2010
Accepted for publication: 25.03.2010

**Adress for correspondence:**
Prof. zw.dr hab.med Krzysztof Simon
Department of Infectious Diseases, Hepatology and Acquired Immune Deficiencies,
Wroclaw University of Medicine, Poland
ul. Koszarowa 5, 51-149 Wrocław, Poland
e-mail: krzysimon@poczta.onet.pl