



UNIVERSITAS INDONESIA

VARIABILITAS DAN DISTRIBUSI SUBTIPE HIV-1, SERTA
HUBUNGANNYA DENGAN KARAKTER DEMOGRAFI, DARI
POPULASI HIV POSITIF DI INDONESIA, DALAM KURUN
WAKTU TAHUN 1993 - 2000

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ERLIN LISTIYANINGSIH
NPM : 7000010583

PROGRAM STUDI ILMU KESEHATAN MASYARAKAT
PROGRAM PASCASARJANA
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WAKTU TAHUN 1993 - 2000**

**Tesis ini diajukan sebagai
Salah satu syarat untuk memperoleh gelar
MAGISTER KESEHATAN**

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STUDI ILMU KESEHATAN MASYARAKAT
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Tesis, Januari 2003

ERLIN LISTIYANINGSIH

Variabilitas dan Distribusi Subtipe HIV-1, serta Hubungannya dengan Karakter Demografi, dari Populasi HIV Positif di Indonesia, dalam Kurun Waktu Tahun 1993 - 2000

xvii + 92 halaman, 24 tabel, 9 gambar, dan 2 lampiran

ABSTRAK

Epidemi HIV di negara-negara Asia terjadi lebih lambat bila dibandingkan dengan negara-negara belahan dunia yang lain. Sejak mulai ditemukan kasusnya yang pertama (tahun 1987), epidemi HIV di Indonesia relatif stabil. Namun, sejak kurang lebih empat (4) tahun yang lalu (tahun 1998) menurut laporan Ditjen P2MPLP DepKes RI telah terjadi lonjakan insiden kasus HIV positif per tahun secara mengkhawatirkan terutama pada kelompok resiko tertular secara kontak seksual. Beberapa hasil penelitian akhir-akhir ini mengatakan adanya kondisi '*emerging epidemic*' HIV pada kelompok resiko heteroseksual.

Untuk lebih dapat meningkatkan upaya pencegahan penularan dan penatalaksanaan penderita, serta memperkirakan kelanjutan epidemi yang akan terjadi, perlu dilakukan karakterisasi epidemi HIV yang sedang berlangsung di Indonesia pada beberapa periode terakhir terutama dalam hubungannya dengan terjadinya kenaikan tajam kasus-kasus yang telah dilaporkan.

Penelitian ini dilakukan dengan metode *Case-Series*, berlangsung selama tujuh tahun mulai tahun 1993 hingga 2000, dengan populasi sampel adalah individu-individu yang telah terinfeksi HIV dari daerah epidemi Jakarta, Papua, Bali, dan beberapa kasus dari daerah epidemi lain. Kasus-kasus HIV positif tersebut sebagian besar (66 %) berasal

dari suku Jawa, 13 % dari suku Papua asli, dan 11 % dari suku Bali, dan hampir semua berada pada usia reproduktif yang tertular HIV dengan cara kontak seksual (98 %), dengan proporsi kasus laki-laki (56 %) sedikit lebih tinggi dari pada proporsi kasus perempuan (44 %).

Hasil pemeriksaan teknik PCR (Polymerase Chain Reaction) dan RT-PCR (Reverse Transcription Polymerase Chain Reaction) diketahui bahwa di Indonesia, dalam masa penelitian terjadi pergeseran corak sub tipe. Pada awal penelitian hanya ditemukan sub tipe B, kemudian berkembang dengan ditemukannya sub tipe E maupun sub tipe B/E dengan proporsi yang terus meningkat. Analisa keserupaan genetik dengan menggunakan teknik Heteroduplex Mobility Assay (HMA) menunjukkan bahwa HIV-1 di Indonesia mempunyai keserupaan genetik dengan strain referensi HIV-1 dari Thailand, USA, Central African Republic, Brazil, dan India.

Untuk melihat hubungan antara sub tipe HIV-1 dengan variabel-variabel penelitian dilakukan analisa statistik bivariat dan multivariat. Sub tipe HIV-1 pada populasi kasus HIV positif pada penelitian ini berhubungan statistik bermakna dengan lokasi penemuan kasus, tetapi tidak dengan suku, umur maupun jenis kelamin. Populasi kasus HIV positif dari lokasi Papua berpeluang 6,4 kali (95% CI = 1,52 – 26,98) untuk memiliki sub tipe E HIV-1, tetapi 0,05 kali peluangnya untuk memiliki sub tipe B HIV-1, bila dibandingkan dengan populasi kasus HIV positif dari lokasi Bali. Populasi kasus HIV positif bersuku Papua mempunyai kemungkinan 3,06 kali lebih tinggi (95 % CI = 0,823 – 11,375) memiliki sub tipe E HIV-1, dan 0,24 kali lebih rendah (95 % CI = 0,02 – 1,24) memiliki sub tipe B HIV-1 dari pada populasi HIV positif bersuku bukan Papua. Peluang untuk mencapai status AIDS pada kasus HIV positif dengan sub tipe E lebih rendah 0,21 kali (95% CI = 0,046 – 0,959) bila dibandingkan dengan peluang kasus HIV positif dengan sub tipe B. Progresifitas kearah AIDS pada kasus-kasus HIV pada penelitian ini memiliki hubungan statistik yang bermakna dengan sub tipe HIV-1, tetapi tidak dengan lokasi penemuan, suku, umur, maupun jenis kelamin kasus.

Daftar bacaan : 109 (1987-2002)

**POST GRADUATE
PUBLIC HEALTH STUDY
REPRODUCTION HEALTH PROGRAM**

Thesis, Januari 2003

ERLIN LISTIYANINGSIH

Subtype Variability of Human Immunodeficiency Virus Type-1 and Their Relationship to the Demographic Characteristic of Indonesian HIV Cases, from 1993 to 2000

xvii + 92 pages, 24 tables, 9 pictures, 2 addendum

ABSTRACT

HIV epidemic in Asia arrived relatively late, and HIV infection is still confined largely to population known to be at high risk (IDU, sex workers, and men who have sex with men). However there is dramatic increase of the HIV infection incidence rate among high-risk population in several Asian Countries since past few years, Indonesia is the one example. While HIV-1 subtype E is the most prevalent strain than other subtype circulating in Southeast Asia, little is known about genetic subtype of HIV-1 responsible for the fulminating epidemic in Indonesia.

Here we *gp41 env* RT-PCR and *gp120 env* HMA subtyped the isolates of a case-series of 255 HIV cases identified in high prevalence regions of Indonesia between 1993 and 2000, and then investigated the correlation between genetic subtype to multiple demographic characteristics and disease progression using bivariate and multivariate analysis. Most (98%) of the cases resulted from sexual contact, and 2% from vertical transmission; 56% are male and 44% are female. The ethnicity of the cases is Javan (66%), Balinese (11%) and Papuan (13%). 67% of the female cases and 14% percent of the male cases were commercial sex workers. 14% of the male cases were military and 8 % of the female cases were housewives.

In 1993/94 only subtype-B viruses were observed, but by 1996 subtype-E had become, and remains, the major circulating subtype. It is suggested that HIV-1 subtype

circulates in Indonesia has shifted from HIV-1 subtype B to HIV-1 subtype-E, indicate that HIV-1 subtype-E is the most transmissible and prevalent HIV-1 subtype through heterosexual contact in Indonesia. However, subtype-B virus remains the most prevalent in Bali. HMA analysis identified isolates having homology to subtype-B isolates BR20 (Brazil), TH14 (Thailand) and SF162 (USA) during 1993/94, then broadening to include subtype-E isolates TH22 (Thailand), TH06 (Thailand) and CAR7 (Central African Republic). In 2000, two isolates homologous to IN868 (India) were identified in Papuan samples.

No correlation was observed between gp41-established subtype and age, gender, or ethnicity, but location. The probability of having HIV-1 subtype-E among HIV infected people in Papua was measured to be 6.4 times greater (95% CI = 1,52 – 26,98) than in Bali, whereas the probability of having HIV subtype-B among HIV infected people in Bali is 20 times greater than in Papua and 4.7 times greater than Jakarta. Papuans were observed to have 3.06 times greater probability (95% CI = 0.823 – 11.375) of having a subtype-E infection than non-Papuan, and smaller probability (OR = 0.24 ; 95% CI = 0.054 – 1.769) of having a subtype-B infection than non-Papuans.. HIV cases with subtype-E HIV-1 were observed to have 0,21 times probability to progress to AIDS (95% CI = 0.046 – 0.959) than probability of HIV cases with subtype B HIV-1 in Indonesia. Disease progression was observed to correlate to HIV-1 subtype, but not age, gender, ethnicity, nor location.

Reference : 109 (1987-2002)

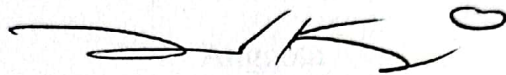
PERNYATAAN PERSETUJUAN

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Program Pascasarjana Universitas Indonesia

Depok, Januari 2003

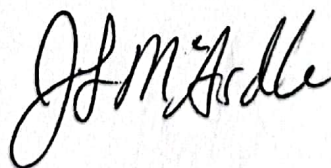
Komisi Pembimbing

Ketua
(Pembimbing Utama)



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Pembimbing II



(Lt. James McArdle PhD)

**PANITIA SIDANG UJIAN TESIS MAGISTER
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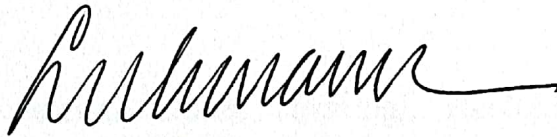
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Ketua

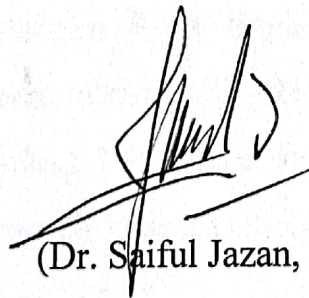


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DAFTAR PUSTAKA

- Anderson DJ, O'Brien TR, Politch JA, et al., 1992
Effect of Disease Stage and Zidovudin Therapy on the Detection of HIV Type 1 in Semen. *JAMA*. 267(20):2769-74.
- Artenstein AW, Vancott TC, Mascola JR, et al., 1995
A Dual infection with human immunodeficiency virus type 1 of distinct envelope subtypes in human. *J Inf Dis*. 71:805-81.
- Barin F, Courouce AM, Pillonel J, et al., 1997
Increasing diversity of HIV-1 M serotypes in French blood donors over a 10-year period (1985-1995). Retrovirus Study Group of the French Society of Blood Transfusion. *AIDS*. 11(12):1503-8.
- Baum MK, Shor-Posner G, Lu Y, et al., 1995
Micronutrients and HIV-1 disease progression. *AIDS*. 9:1051-1056
- Bruce C, Clegg C, Featherstone A, et al., 1994
Presence of multiple genetic subtypes of human immunodeficiency virus type 1 proviruses in Uganda. *AIDS Res Hum Retroviruses*. 10(11):1543-50
- Belda FJ, Barlow KL, Murphy G, et al., 1998
A Dual Subtype B/E HIV type 1 Infection with a Novel V3 Loop Crown Motif among Infections Acquired in Thailand and Imported into England. *AIDS Research And Human Retroviruses*. 14 (10):911-916
- Berger EA, Doms RW, Fenyo EM, et al., 1998
A New Classification for HIV-1. *Nature*. 391(6664):240
- Blair J, Hanson D, Jones J, et al., 2000
Do Gender Differences in Viral Load Predict Differences in HIV Disease Progression ?. Abstract # 192. *Retrovirus Conference* , January, 2000.
- Bleul CC, Wu L, Hoxie JA, et al., 1997
The Coreceptors CXCR4 and CCR5 are differentially expressed and regulated on human T lymphocytes. *Proc Natl Acad Sci USA*. 94(5):1925-1930
- Carrington M, Nelson GW, Martin MP, et al., 1999
HLA and HIV-1: Heterozygote Advantage and B*35-Cw*04 Disadvantage. *Science*. 283(5408):1748-1752

- Cassol S, Weniger BG, Babu G, et al., 1996
Detection of HIV type 1 *env* Subtypes A, B, C, and E in Asia Using Dried Blood Spots: A New Surveillance Tool for Molecular Epidemiology. *AIDS Research and Human Retroviruses*. 12 (15):1435-1441
- Castro BA, Cheng MC, Evans LA, et al., 1998
HIV heterogeneity and viral pathogenesis. *AIDS*. 2 (suppl 1):S17-S27
- Clavel F, Mansinko S, Chamaret MA, 1987
Human Immunodeficiency virus type 2 infection associated with AIDS in West Africa. *N Engl J Med*. 316:1180-1185
- Coffin JM, 1990
The virology of AIDS: 1990. *AIDS*. 4(suppl 1):S1-S8
- Coffin JM, 1992
Structure and Classification of Retroviruses. *In The Retroviridae*. Edited by Levy JA. New York: Plenum Press. 19-49
- Cohen OJ, Paolucci S, Bende SM, et al., 1998
CXCR4 and CCR5 Genetic Polymorphisms in Long-Term Nonprogressive Human Immunodeficiency Virus Infection: Lack of Association with Mutations other than CCR5- δ 32. *Journal of Virology*. 6215-6217
- Connor R, Ho D, Kuritzkes D, et al., 1994
Human Immunodeficiency Virus. *Textbook of Virology*. 707-754
- Connor RI, Ho DD, 1994
Etiology of AIDS: Biology of Human Retroviruses. *The Virology*. 13-38
- Cornelissen M, Kampinga G, Zorgdrager F, et al., 1996
Human Immunodeficiency Virus Type 1 Subtype Defined by *env* Show High Frequency of Recombinant *gag* Genes. *Journal of Virology*. 70 (11):8209-8212
- Dean M, Carrington M, Winkler C, et al., 1996
Genetic restriction of HIV-1 infection and disease progression to AIDS by deletion allele of the CCR5 structural gene. *Science*. 273:1856-1862
- Delmas MC, Jadand C, De Vincenzi I, et al., 1997
Gender differences in CD4+ cell count persist after HIV-1 infection. SEROCO Study Group. *AIDS*. 11:1071-1073
- Diaz RS, Zhang L, Bush MP, et al., 1997
Divergence of HIV-1 quasispecies in an epidemiologic cluster. *AIDS*. 11:415-422

Di Marzio P, Tse J, Landau NR, 1998

Chemokine receptor regulation and HIV type 1 tropism in monocyte-macrophages. *AIDS Res Hum Retroviruses*. 14(2):129-138

_____, 2000

Perkembangan Penyakit HIV/AIDS di Indonesia. Direktorat Jendral P2MPLP Dep Kes RI

_____, Surveillance Report, June 30, 2001

HIV-1 subtypes in Canada. Population and Public Health Branch, MOH, Canada

Eric L. Delwart, Belinda Herring, Gerald H., et al., 1994

Heteroduplex Mobility Analysis HIV-1 *env* Subtyping Kit Protocol Version 3. *NIH AIDS Research and Reference Reagent Program* 1994

Forster R, Kremmer E, Schubel A, et al., 1998

Rapid internalization and recycling upon activation. *J Immunol*. 160(3):1522-1531

Fultz PN, Yus L, Wei Q, et al., 1997

Human Immunodeficiency Virus Type 1 Intersubtype (B/E) Recombination in a Superinfected Chimpanzee. *Journal of Virology*. 71 (10):7990-7995

Galai N, Kalinkovich A, Burstein R, et al., 1997

African HIV-1 subtype C and rate of progression among Ethiopian immigrants in Israel. *Lancet*. 349(9046):180-181

Gao F, David L, Robertson, et al., 1996

The Heterosexual Human Immunodeficiency Virus Type 1 Epidemic in Thailand Is Caused by Intersubtype (A/E) Recombinant of African Origin. *Journal of Virology*. 70 (10):7013-7029

Gonzalez E, 2001

Global survey of genetic variation in CCR5, RANTES and MIP-1 alpha: impact on the epidemiology of the HIV-1 pandemic. *Proc Natl Acad Sci USA*. 98(9):5199-204

Gottlieb S, 1998

New, more virulent strain of HIV found. *Nature Medicine*. 9:1032-6

Gunawan S, 2001

AIDS di Asia Pasifik Masalah dan Penanggulangannya. Seminar sehari 'Informasi Terkini dari ICAAP VI Melbourne'.

Gunawan S, 2001

Kecenderungan Peningkatan Kasus HIV/AIDS Di Indonesia. Seminar sehari-hari 'Penyakit Emerging di Indonesia; Ancaman dan Penanggulangannya'

Gupta P, Lerous C, Patterson CK., et al., 2000

Human Immunodeficiency Virus Type 1 Shedding Pattern in Semen Correlates with the Compartmentalization of Viral Quasi Species Between Blood and Semen. *J of Infectious Diseases*. 182(1):79-87

Gupta SK, Lysko PG, Pillarisetti K., et al., 1998

Chemokine receptors in human endothelial cells – functional expression of CXCR4 and its transcriptional regulation by inflammatory cytokines. *J Bio Chem*. 273(7):4282-4287

Graneli PA, Moser B, Pope M., et al., 1996

Efficient interaction of HIV-1 with purified dendritic cells via multiple chemokine coreceptors. *J Exp Med*. 184(6):2433-2438

Haseltine WA, Wong SF, 1998

The molecular biology of the AIDS virus. *Sci Am*. 259:34-42

Huang Y, Paxton WA, Wolinsky SM, et al., 1996

The role of mutant CCR5 allele in HIV-1 transmission and disease progression. *Nat Med*. 2:1240-1243

Hu DJ, Buve A, Baggs J, et al., 1999

What role does HIV-1 subtype play in transmission and pathogenesis? An epidemiological perspective. *AIDS*. 13:873-881

Hu DJ, Dondero TJ, Rayfield MA, et al., 1996

The emerging genetic diversity of HIV. The importance of global surveillance for diagnostics, research, and prevention. *JAMA*. 275(3):210-6

Jeannot M, Sztajzel R, Carpentier N, et al., 1989

HLA Antigens Are Risk Factors for Development of AIDS. *Journal of Acquired Immune Deficiency Syndromes*. 2:28-32

Kaleebu P, French N, Mahe C, et al., 2002

Effect of Human Immunodeficiency Virus (HIV) type 1 Envelope Subtypes A and D on Disease Progression in a Large Cohort of HIV-1-Positive Persons in Uganda. *J of Infectious Diseases*. 185:1244-50

Kalish ML, Baldwin A, Raktham S, et al., 1995

The evolving molecular epidemiology of HIV-1 envelope subtypes in injecting drug users in Bangkok, Thailand: implications for vaccine trials. *AIDS*. 9:851-857

- Kanki PJ, Hannel DJ, Sankale JL, et al., 1999
Human Immunodeficiency virus type 1 subtypes differ in disease progression. *J of Infectious Diseases*. 179:68-73
- Kevin R. Porter, John R. Mascola, Hudoyo Hupudio, et al., 1997
Genetic, Antigenic and Serologic Characterization of Human Immunodeficiency Virus Type 1 from Indonesia. *J of Acquired Immune Deficiency Syndromes and Human Retrovirology*. 14 (1):1-6
- Kostrikis LG, Huang Y, Moore JP, et al., 1998
A Chemokine receptor CCR2 allele delays HIV-1 disease progression and is associated with CCR5 promoter mutation. *Nat Med*. 4:350-353
- Kostrikis LG, Tyagi S, Mhlanga MM, et al., 1998
Spectral genotyping of human alleles. *Science*. 279:1228-29
- Lavi E, Strzki JM, Ulrich AM, et al., 1997
CXCR4 (Fusin), A Co-receptor for type 1 human immunodeficiency virus (HIV-1), is expressed in the human brain in a variety of cell types, including microglia and neurons. *Am J Pathol*. 151(4):1035-42
- Lewin SR, Suzane MC, 1994
AIDS pathogenesis. *AIDS*. 8(suppl 2):S3-S11
- Lifson AR, 1990
The epidemiology of AIDS and HIV infection. *AIDS*. 4(suppl 1):S23-S28
- Liu R, Paxton W, Choe S, et al., 1996
Homozygous defect in HIV-1 coreceptor accounts for resistance of some multiply-exposed individuals to HIV-1 infection. *Cell*. 86:367-377
- Long EM, Martin HL, Kreiss JK, et al., 2000
Gender differences in HIV-1 diversity at time of infection. *Nature Medicine*. 6:71-75
- Louisiriro'chanakul S, Beddows S, Cheingsong R, et al., 1999
Role of Maternal Humoral Immunity in Vertical Transmission of HIV-1 Subtype E in Thailand. *AIDS Journal of Acquired Immune Deficiency Syndromes*. 21:259-265
- Louwagie J, McCutchan FE, Peeters M, et al., 1993
Phylogenetic analysis of gag genes from 70 international HIV-1 isolates provides evidence for multiple genotypes. *AIDS*. 7 (6):769-780

- Magierowska M, Theodorou I, Debre P, et al., 1999
Combined genotypes of CCR5, CCR2, SDF-1, and HLA genes can predict the long-term nonprogressor status in human immunodeficiency virus-1-infected individuals. *Blood*. 93:936-41
- MacDonald K, Embree JE, Nico JD, et al., 2001
The HLA A2/6802 Supertype Is Associated with Reduced Risk of Perinatal Human Immunodeficiency Virus Type 1 Transmission. *J of Infectious Diseases*. 183:503-6
- Mangano A, Gonzalez E, Dhanda R, et al., 2001
Concordance between the CC Chemokine Receptor 5 Genetic Determinants That Alter Risks of Transmission and Disease progression in Children Exposed Perinatally to Human Immunodeficiency Virus. *J of Infectious Diseases*. 183:1574-85
- Mangano A, Kopka J, Batalla M, et al., 2001
Protective effect of CCR2-641 and not of CCR5-delta32 and SDF1-3'A in pediatric HIV-1 infection. *J Acquir Defic Syndr*. 23(1):52-7
- Martin HL, Richardson BA, Nyange PM, et al., 1999
'Vaginal' lactobacilli, microbial flora, and risk of human immunodeficiency virus type 1 and sexually transmitted disease acquisition. *J of Infectious Diseases*. 180(6):1863-8
- Mascola JR, Louwagie J, McCutchan FE, et al., 1994
Two antigenically distinct subtypes of human immunodeficiency virus type 1 viral genotype predict neutralization serotype. *J of Infectious Diseases*. 169:48-54
- McDermott DH, Zimmerman PA, Guignard F, et al., 1998
CCR5 promoter polymorphism and HIV-1 disease progression. *Lancet*. 352:866-70.
- McNicholl JM, 1997
Host genes and HIV: the role of the chemokine receptor gene CCR5 and its allele. *Emerging Infectious Disease*. 3(3):261-71
- Michael NL, Louie LG, Rohrbaugh AL, et al., 1997
The role of CCR5 and CCR2 polymorphisms in HIV-1 Transmission and disease progression. *Nat Med*. 3(10):1160-2
- Miller CJ, 1998
Host and viral factors influencing heterosexual HIV transmission. *Journal of Reproduction and Fertility*. 3:42-51

- Misrahi M, Teglas JP, N'Go N, et al., 1998
CCR5 Chemokine Receptor Variant in HIV-1 Mother-to-Child Transmission and Disease Progression in Children. *JAMA*. 279(4):277-80
- Muller-Trutwin MC, Chaix ML, Letourneur F, et al., 1999
Increase of HIV-1 subtype A in Central African Republic. *J Acquir Immune Deficiency Syndrome*. 21(2):164-71
- Mummidi S, 1998
Genealogy of the CCR5 locus and chemokine system gene variants associated with altered rates of HIV-1 disease progression. *Nature Medicine*. 4(7):786-793
- Murray MCM, Embree JE, Ramdahin SG, et al., 2000
Effect of Human Immunodeficiency Virus (HIV) type 1 Viral Genotype on Mother-to-Child Transmission of HIV-1. *J of Infectious Diseases*. 181:746-749
- Myers G, Korber B, Wain-Hobson S, et al., 1993
Human retroviruses and AIDS 1993. Los Alamos, NM: Los Alamos National Laboratory.
- Neilson JR, John GC, Carr JK, et al., 1999
Subtypes of human immunodeficiency virus type 1 and disease stage among women in Nairobi, Kenya. *J Infectious Diseases*. 179:68-73
- Noya G, Kalinkovich A, Burstein R, et al., 1997
African HIV-1 subtype C and rate of progression among Ethiopian immigrant in Israel. *Lancet*. 349: 180-181
- O'Brien SJ, Moore JP, 2000
The effect of genetic variation in chemokines and their receptors on HIV transmission and progression to AIDS. *Immunol Review*. 177:p.99-111.
- Ohshige K, Morio S, Mizushima S, et al., 2000
Behavioural and serological human immunodeficiency virus risk factors among female commercial sex workers in Cambodia. *International Journal of Epidemiology*. 29:344-354
- Osmanov S, Heyward WL, Esparza J, 1997
HIV-1 Genetic Variability: Implications for the Development of HIV Vaccines. *UNAIDS-WHO*, Division of Research and Intervention Development

- Ou CY, Takebe Y, Weniger BG, et al., 1993
Independent introduction of two major HIV-1 genotypes into distinct high-risk populations in Thailand. *Lancet*. 341:1171-4
- Overbaugh J, Kreiss J, Poss M, et al., 1999
Studies of human immunodeficiency virus type 1 mucosal viral shedding and transmission in Kenya. *J of Infectious Diseases*. 179(suppl 3):S401-4
- Pepin J, Morgan G, Dunn D, et al., 1991
HIV-2 immunosuppression among asymptomatic West African prostitutes: evidence that HIV-2 is pathogenic, but less so than HIV-1. *AIDS*. 5:1165-1172
- Peterlin BM, Luciw PA, 1988
Molecular biology of HIV. *AIDS*. 2 (suppl 1): S29-S40
- Periquet BA, Jammes NM, Lambert WE, et al., 1995
Micronutrient levels in HIV-1-infected children. *AIDS*. 9:887-893
- Philpott S, 1999
CCR5 genotype and resistance to vertical transmission of HIV-1. *Journal of Acquired Immune Deficiency Syndromes and Human Retrovirology*. 21(3):189-193
- Phyllis JK, 1992
Virologic and Biologic Features of HIV-2. *AIDS and Other Manifestations of HIV Infection*. Second Ed. Raven Press, Ltd, New York.
- Pillay D, Walker AS, Gibb DM, et al., 2002
Pediatric HIV Infection: Disease Progression and Responses to Therapy. Abstrac No 813W. 9th Conference on Retroviruses and Opportunistic Infections 2002.
- Program for the Collaboration Against AIDS and Related Epidemics (ProCAARE):
Long-term non-progression of HIV infection and factors affecting disease progression. , 24 February 2002.
- Quinn TC, Wawer MJ, Sewankambo MB, et al., 2000
Viral Load and Heterosexual Transmission of Human Immunodeficiency Virus Type 1. *The New England Journal of Medicine*. 342(13):921-9
- Renjifo B, Fawzi W, Mwakagile D, et al., 2001
Differences in Perinatal Transmission Among Human Immunodeficiency Virus Type 1 Genotypes. *Journal of Human Virology*. 4:16-25
- Robertson DL, Sharp PM, McCutchan FE, et al., 1995
Recombination in HIV-1. *Nature*. 374:124-126

- Samson M, Libert F, Doranz BJ, et al., 1996
Resistance to HIV-1 infection in Caucasian individuals bearing mutant alleles of the CCR-5 chemokine receptor gene. *Nature*. 382:722-725
- Schacker T, Ryncarz AJ, Goddard J, et al., 1998
Frequent recovery of HIV-1 from genital herpes simplex virus lesion in HIV-1-infected men. *JAMA*. 280:61-66
- Sela M, 1990
Immunology in AIDS in 1990. *AIDS*. 4(suppl 1):S9-S14
- Sherefa K, Johansson BO, Salminen M, et al., 1998
Full-Length Sequence of Human Immunodeficiency Virus Type 1 subtype A, Recombined with Subtype C in the env V3 Domain. *AIDS Research And Human Retroviruses*. 14 (3):289-292
- Shioda T, Oka S, Xin X, et al., 1997
In Vivo Sequence Variability of Human Immunodeficiency Virus Type 1 Envelope gp120: Association of V2 Extension with Slow Disease Progression. *Journal of Virology*. 4871-4881
- Smith MW, Dean M, Carrington M, et al., 1997
Contrasting genetic influence of CCR2 and CCR5 variants on HIV-1 transmission and disease progression. *Science*, 277:959-965
- Soto-Ramirez LE, Renjifo B, McLane MF, et al., 1996
HIV-1 Langerhans' Cell Tropism Associated with Heterosexual Transmission of HIV. *Science*. 271:1291-1293
- Stephenson J, 2001
Swift Action Needed to Prevent Explosive HIV/AIDS Epidemics in Asia. *JAMA*. 286(16):
- Sterling TR, Lyles CM, Vlahov D, et al., 1999
Sex differences in longitudinal human immunodeficiency virus type 1 RNA level among seroconverters. *Journal of Infectious Diseases*. 180:666-672
- Sterling TR, Vlahov D, Amtemborski J, et al., 2001
Initial HIV-1 RNA level and progression to AIDS in women and men. *N England J Med*. 2001
- Subbarao S, Vanichseni S, Hu DJ, et al., 2000
Genetic characterization of incident HIV type 1 subtype E and B strains from a prospective cohort of injecting drug users in Bangkok, Thailand. *AIDS Res Hum Retroviruses* 16:699-707

- Tachet A, Dulioust E, Salmon D, et al., 1999
Detection and quantification of HIV-1 in semen: identification of a subpopulation of men at high potential risk of viral sexual transmission. *AIDS*. 13:823-31
- Van Harmelen J, Wood R, Lambrick M, et al., 1997
An association between HIV-1 subtypes and mode of transmission in Cape Town, South Africa. *AIDS*. 11(1):81-7
- Van Rij RP, 1999
Reduced prevalence of the CCR5 delta 32 heterozygous genotype in human immunodeficiency virus-infected individuals with AIDS dementia complex. *Journal of Infectious Diseases*. 18(3):854-857
- Wainberg MA, Friedland G, 1998
Public Health Implications of Antiretroviral Therapy and HIV Drug Resistance. *JAMA*. 279(24):1977-83
- Wasi C, Herring B, Raktham S, et al., 1995
Determination of HIV-1 subtypes in injecting drug users in Bangkok, Thailand, using peptide-binding enzyme immunoassay and heteroduplex mobility assay: evidence of increasing infection with HIV-1 subtype E. *AIDS*. 9(8):843-9
- Weniger BG, Takebe Y, Ou CY, et al., 1994
The molecular epidemiology of HIV in Asia. *AIDS*. 8 (suppl 2):S13-S28
- Weiss RA, 1993
How Does HIV Cause AIDS?. *Science*. 260:1273-78
- Winkler C, 1998
Genetic restriction of AIDS pathogenesis by an SDF-1 chemokine gene variant. *Science*. 279:387-391
- Winkler C, Modi W, Smith MW, et al.,
Genetic restriction of AIDS pathogenesis by an SDF-1 chemokine gene mutation. *Science*. In press.
- WISE words, 2000
Women and Disease Progression. *The Body: An AIDS and HIV Information Resource*. Issue #6, October, 2000

Yanjie Y, 1999

Role of CXCR4 in cell-cell fusion and infection of monocyte-derived macrophages by primary human immunodeficiency virus type 1 (HIV-1) strains: two distinct mechanisms of HIV-1 dual tropism. *Journal of Virology*. 73(9):7117-7125.