13-68
AP - 9/24/13
Senate Info - 10/8/13

Undergraduate Distance Education Review Form
(Required for all courses taught by distance education for more than one-third of teaching contact hours.)

Existing and Special Topics Course

Course: BIOL 117 Understanding HIV Biology and AIDS

Instructor(s) of Record: Bharathan Narayanaswamy

Phone: 7-2584 **Email:** Bharathn@iup.edu

Step Two: Departmental/Dean Approval

Recommendation: ☒ Positive (The objectives of this course can be met via distance education)

☐ Negative

[signature] 9/13/13

Signature of Department Designee Date

Endorsed: [signature] 9/18/13

Signature of College Dean Date

Forward form and supporting materials to Liberal Studies Office for consideration by the University-wide Undergraduate Curriculum Committee. Dual-level courses also require review by the University-wide Graduate Committee for graduate-level section.

Step Three: University-wide Undergraduate Curriculum Committee Approval

Recommendation: ☒ Positive (The objectives of this course can be met via distance education)

☐ Negative

Gail Eschrich 9/25/13

Signature of Committee Co-Chair Date

Forward form and supporting materials to the Provost within 30 calendar days after received by committee.

Received

SEP 16 2013

Liberal Studies

Step Four: Provost Approval

☑ Approved as distance education course ☐ Rejected as distance education course

Signature of Provost 9/26/13 Date

Forward form and supporting materials to Associate Provost.

Table of Contents

Narrative Rationale Items A1-A5

1. How is/are the instructor(s) qualified in the distance education delivery method as well as the discipline?

Bharathan has sought professional development in online course design and pedagogy. Since December 2012, he has participated in biweekly consultations with IUP's instructional design staff to discuss both the design of the online course, potential teaching strategies, and technologies available for course delivery. The instructor also completed the Desire2Learn Boot Camp offered by the IUP IT Support Center.

Bharathan has participated in the development of technology-enhanced learning opportunities. In 2006-07, the instructor worked closely with instructional designers and production staff from Concurrent Technologies Corporation (CTC) on a Department of Defense grant project Developing Basic Biology Operations (SDR 111) class online. Currently, the instructor uses several online resources for this course and other courses. Bharathan also received a National Science Foundation Instrumentation and Laboratory Improvement grant for a server to use online resources in his Principles of Biology I (BIOL 111) course.

Bharathan has over twenty years of experience in the field of biology. He has been teaching at IUP since 1997 and holds a PhD from the University of Maine.

2. How will <u>each objective</u> in the course be met using distance education technologies?

General overview: Course modules will require students to watch narrated lectures (10 minutes or less) and read chapters in the textbook and essays. As part of the modules, students will complete self-tests to help them and the instructor gauge their understanding and progress. Also, students will also participate in both small- and large-group discussions on the LMS forums, enabling the instructor to assess their higher level learning and to provide feedback to students. Throughout the course, the instructor will interact with the students through the LMS, as well as via Skype, e-mail, and telephone as the need dictates. Students will be assessed through the completion of the final exam, case studies, and critiques.

<u>Objective 1:</u>

Describe and analyze the general characteristics of HIV transmission as a means to interpret the Biology of the virus.

Students must gain an understanding of general infection cycle of viruses and more specifically HIV infection on immune cells of the body such as CD-4 cells. This understanding provides a basis for the rest of the course as students explore scientific and medical theories including development of a vaccine for HIV throughout the past four decades. This material involves basic virology and knowledge of the circulatory system and immunology and is best delivered through short narrated lectures and

animations on the LMS. Given the importance of this material and its relationship to the remaining course content, students must past the self-test related to this material. There will be opportunities for all students to interact synchronously with the professor through chat, Skype, or the telephone.

Objective 2:

Compare how general virus transmission has been perceived throughout the ages by identifying the common and uncommon modes of transmission of HIV and AIDS.

Textbook resources and short lectures delivered via the LMS will enable students to follow the development of our understanding and perception of HIV and AIDS over the last 40 years. Specifically, students will study the common modes of virus transmission (air-borne, water, vector and non-vector, and blood). Students will complete self-assessments and participate in small-group forum discussions to receive feedback on their understanding of the concepts. Students will demonstrate attainment of this objective through completion of the final exam, case studies, and the critique.

Objective 3:

Describe how HIV infection and AIDS is perceived and dealt with in today's society.

Students will take an HIV/AIDS assessment survey on the first day of class which has them describe their level of understanding of the HIV/AIDS infection. The same survey will then be given during the last module with small-group and full-group discussions to follow. Readings and course materials will emphasize how the individual affected by HIV and AIDS is stigmatized in society and the disproportionate transfer among individuals of different social, ethnic, and economic groups. Students will develop a case study (sample will be available in the LMS) based on some aspect of how HIV and AIDS infection is perceived globally and the demographic impact of HIV and AIDS across the family and household life-cycle. Students will demonstrate attainment of this objective through critiques of both student case studies and the non-textbook reading.

Objective 4:

Assess historical figures in last 40 years who have made contributions to our understanding of HIV and AIDS.

Students will read a series of articles and chapters in the textbook about historical figures who have made significant contributions to our understanding of HIV and AIDS, tracing our understanding of the distribution of HIV among individuals and populations. This material is covered and students will have opportunity for feedback throughout the course through the class discussions. Students will be assessed on this objective through the Final Exam and the completion of the Case Studies.

3. How will instructor-student and student-student, if applicable, interaction take place?

Chat—The instructor will have set times as well as any specific times a student will need for synchronous chat. Times will be posted in the LMS. Different dates and times will be used to ensure all students can participate.

Forum—The instructor will use the forum for asynchronous interactions with the students. Students will be required as part of the course modules to participate in asynchronous discussions about the course topics. Students will take turns leading and facilitating these discussions among their fellow group members of assigned readings and resources. The instructor will facilitate the process, provide guidance to the group leaders in facilitating the discussions, and to provide commentary and feedback to the discussion groups as needed.

The instructor will also offer virtual and on-campus office hours to assist students as needed. During these times, the instructor will be available via chat, phone, and Skype. The instructor will communicate through e-mail as well.

4. How will student achievement be evaluated?

1. Final Exam (15%)—Students will be required to take a final comprehensive exam on the course content. The exam will consist of multiple choice questions. The exam will take place on the last day of class, and students may only have one attempt.

2. Self-Tests (30%; 5% for each self-test)—Students will be given six multiple-choice self-tests that relate to the material from their readings and the online resources. Self-tests are designed to assess student understanding of the material and to provide them feedback on their understanding. Students will be evaluated on their ability to correctly respond to the questions. Students may take each self-test two times, and must score at least 60% to move on to the next module. Students who do not meet the minimum score should seek consultation with instructor.

3. Case Studies (20%; 10% for each case study)—Students will be given two case studies. These case studies will cover the global impacts of HIV/AIDS, role of anti-retroviral therapies and their opportunities and challenges, the prevention among minority communities, and the risk factors generally associated with HIV transmission. Students must prepare a response to each case study based on the questions provided by the instructor. Students will be evaluated on the case studies based on their ability to summarize the case, respond to questions, and provide a support using textbook and online resources.

4. Forum Discussions (25%; 5% for each discussion)— Students will participate in five small-group, student-led forum discussions throughout the semester. These discussions will cover course resources and materials regarding topics, such as transmission, stigmatization, legal issues, and models of AIDS management. For each discussion, the student leader will facilitate the discussion, in consultation with the instructor, regarding the assigned readings and materials. Students will be

evaluated on their posting frequency, posting quality, and grammar and spelling as outlined in the Group Discussion Rubric.

5. Critique of Non-Textbook Reading (10%)—Students may select one of the supplemental texts for the course to read and write a critique. Critique papers should be a minimum of five pages and demonstrate a connection to the course content, quality of the response, use of technical and descriptive terms associated with HIV/AIDS, and grammar and spelling.

5. How will academic honesty for tests and assignments be addressed?

The following methods will be used to maintain the academic integrity in the course:

Academic Integrity Statement—At the onset of the course, students will be provided with an academic integrity statement in both the course syllabus and the course material. Additionally, all written work will include an academic integrity clause.

Varied Assessments—The course makes use of a variety of assessments and levels of assessment to assure that students have multiple opportunities for feedback and to demonstrate their performance. This also provides the faculty member with ample opportunities to assess student performance.

Written Work—Students will be required to submit their material through Turnitin to assess the authenticity of the work.

Exams and Quizzes—Academic integrity measures for tests and quizzes include the use of large item pools, timed testing, and test security features.

B. Submit to the department or its curriculum committee the responses to items A1-A5, the current official syllabus of record, along with the instructor developed online version of the syllabus, and the sample lesson. This lesson should clearly demonstrate how the distance education instructional format adequately assists students to meet a course objective(s) using online or distance technology. It should relate to one concrete topic area indicated on the syllabus.

BIOL 117 Understanding HIV Biology and AIDS

Syllabus of Record

I. Catalog Description

BIOL 117 Understanding HIV Biology and AIDS 3c-0l-3cr

Prerequisites: Non-Biology department majors and minors only

An introduction to the mode of infection and prevention of AIDS virus which are used as an illustration of biological principles. Profiles biological indicators for HIV disease and its progression to AIDS. Therapeutic and non-therapeutic approaches to treat HIV infections are emphasized. (Does not count toward Biology Electives, Controlled Electives, or Ancillary Sciences for Biology majors and minors.)

II. Course Outcomes and Assessment (Expected Undergraduate Student Learning Outcomes – EUSLO)

Objective 1:

Describe and analyze the general characteristics of HIV transmission as a means to interpret the Biology of virus.

Expected Student Learning Outcomes 1 and 2:

Informed and Empowered Learners

Rationale:

Assignments will require students to have a level of knowledge of circulatory system and immunology that will enable them to understand how these systems work. Assignments will also require students to critically analyze immune systems modalities and to use this analysis to explain how HIV testing is interpreted.

Objective 2:

Compare how general virus transmission has been perceived throughout the ages by identifying the common and uncommon modes of transmission of the HIV and AIDS.

Expected Student Learning Outcome 2:

Empowered Learners

Rationale:

Assignments will require students to evaluate common modes of virus transmission (air-borne, water, vector and non-vector, and blood). In addition, these assignments will engage students in assessing a knowledge base in science and how that knowledge influenced the perception and treatment of individuals infected with HIV.

Objective 3:

Describe how HIV infection and AIDS is perceived and dealt with in today's society.

Expected Student Learning Outcome 3:

Responsible Learners

Rationale:

Assignments will require students to assess their own views of HIV and AIDS infection and how they compare to ethical judgments and social responsibilities in various societies around the world. They will also explore how their personal actions and civic values influence their perception of people having AIDS. Other assignments will have the students analyze AIDS issues in the public realm (e.g. national, state, or local) and to use this analysis to determine how their personal lives are and will be affected.

Objective 4:

Assess historical figures in the last 40 years who have made contributions to our understanding of HIV and AIDS

Expected Student Learning Outcome 1 and 2:

Informed and Empowered Learners

Rationale:

Assignments will require students to gain an understanding of how we have arrived at our current understanding of HIV transmission and prevention by analyzing the distribution of HIV among individuals and populations throughout last three decades. They will then apply these analyses to the evaluation of their own view of HIV transmission and prevention.

III. Course Outline

A. Introduction - What is virus? (3 hours)

1. Biological agents causing diseases in humans
2. How viruses differ from other agents
3. Characteristics of viruses
4. Viruses infecting plants, animals and humans

B. The discovery of HIV and naming the illness (7 hours)

1. AIDS a disease or syndrome
2. Defining the illness: AIDS surveillance

3. Naming of the AIDS virus HIV-1, HIV-2, and HTLV-III

4. Circulatory system—blood, arteries, veins-HIV in blood

5. Immune system—human lymphocytes-T-cells, B-cells

6. Origin of HIV—Biological warfare, virus from cats and old world monkeys

7. Characteristics of HIV—retrovirus, stability of HIV

8. HIV mutations and source of variants

Exam 1 (1 hour)

C. Following virus transmission through the ages – HIV transmission (3 hours)

1. Introduction – virus transmission: an overview

2. Common modes of transmission of HIV—household settings, insects and other Vectors, non-casual transmission

3. HIV in blood, virus load in blood and blood product transmission

4. HIV in Genital fluids, saliva and other body fluids

5. Sexual transmission of HIV, Injection and drug use

6. Maternal-child transmission

D. Preventing the transmission of HIV (3 hours)

1. Quarantine principles and practices

2. Barrier to HIV infection, safer sex—how do I protect myself? Risk factors

3. Education—schools, colleges—Disease prevention and health promotion

4. Blood collection and blood screening for HIV

5. Infection control procedures—AIDS prevention programs

E. Therapy for HIV disease (3 hours)

1. General concept for antimicrobial therapy—treatment vs cure (is there a cure?)

2. anti-HIV therapies—FDA approved drugs, antibody based approach, protease inhibitors

3. Vaccine development—is there a vaccine? Ideal properties of effective vaccine

4. Combination drug AIDS therapy—Opportunities and challenges of drug therapy

Exam 2 (1 hour)

F. Prevalence of HIV infection and AIDS cases in the United States (3 hours)

1. Risk groups and AIDS cases

2. Health care workers

3. Childbearing women, HIV infections in newborns

4. Testing—who should be tested? What does positive test mean?

G. Prevalence of HIV infection and AIDS cases outside the United States—Global prospective (3 hours)

1. Global patterns of HIV transmission and prevalence of AIDS

2. AIDS epidemic in Asia, Africa, and Latin America

3. Economics of preventing HIV infection in developing countries

H. Global strategy to combat the spread of HIV and AIDS (4 hours)

1. Youth—Create educational and economic opportunities—provide formal sexual health education in schools, offering youth friendly health and prevention services

2. Women—Overcome social obstacles to empower women to control their health—create economic opportunities as means to avoid risk behavior, increase access reproductive health care, formation of support groups

3. Men—Work against aggressive social behavior, foster responsible social behavior

4. Role of National Governments working with civil societies and United Nations efforts through WHO

Exam 3 (1 hour)

I. Biological indicators for HIV disease and Progression to AIDS (3 hours)

1. Stages of HIV disease—Asymptomatic stage, chronic stage, AIDS stage

2. Production of HIV specific antibodies

3. Infection of the Central Nervous system

4. Clinical indicators of AIDS diagnosis

J. Endemic, epidemic, and pandemic nature of AIDS (3 hours)

1. A re-evaluation of distribution of AIDS in a global society

2. Pragmatic and multidisciplinary approaches—to prevent spread

3. Role of Government and Gates Foundation in HIV prevention

4. Living with AIDS-Human Dimensions—confronting the news of infection

K. Current studies and models of AIDS management (4 hours)

1. CDC role– current guidelines: Discussion of selected papers from the CDC *HIV/AIDS Prevention among Hispanic/Latino Communities: colloquium "The* DC's Hispanic/Latino Consultation, April 1-2, 2008"

2. A perfect world without HIV and AIDS--HAART

3. An overview of major contributors in the field of HIV research today: David D. Ho, Dennis Burton, and Ben Lewin.

Final exam (four) during final exam week (2 hours)

IV. Evaluation Methods

1. 60% Four examinations (15% for each exam) – three during the semester and a fourth during exam week. Exams will be short answer essays.

2. 20% Four case studies (5% for each exam) - Students will be given four case studies. These case studies will have questions that must be answered and turned in by the student. Each case study will be worth 5% of the final grade.

3. 15% Students will develop one case study for the class. The case study will be based on articles and ideas gathered from sources such as newspapers, newsmagazines, and popular science and medical magazines (e.g. Discover Magazine, Science and Medicine or Journal of the American Medical Association). It will follow the format of the case studies given by the professor and will be worth 15% of their final grade. This will be a class assignment (no presentations in class).

4. 5% Critique of the non-textbook reading. Students will submit a critique with a maximum of five printed pages.

V. Grading Scale

Grading scale: A: 90-100%; B: 80-89%; C: 70-79%; D: 60-69%; F: 59% and below

VI. Undergraduate Course Attendance Policy

The IUP attendance policy will be followed.

VII. Required Textbook

Gerald J. J. Stine. 2012. ***AIDS Update:*** *An annual Overview of Acquired Immune Deficiency syndrome.* ISBN13: 9780073527659 McGraw Hill Publishers

Supplemental Non-textbook reading

Barnett, T., and Whiteside, A., 2006. *AIDS in the Twenty-First Century: Disease and Globalization.* ISBN10: 1403997683. Palgrave **Publishers**

Hung, F., Conner, R., and Villarreal, L., 2012. *AIDS Science and Society* ISBN 0-7637-0086. Bartlett Publishers

Shelby, R.D., Aronstein, D.M. and Thompson, B.J., 1998. *HIV And Social Work: A Practitioner's Guide (Psychosocial Issues of HIV/AIDS)* ISBN10: 1560239069. Haworth Press, Inc.

Suggested Readings

Carpenter, C.C., Fischl, M.A.,Hammer, S.M., Hirsch, M.S., Jacobsen, D.M., Katzenstein, D.A., Montaner, J.S., Richman, D.D., Saag, M.S., Schooley, R.T.,Thompson, M.A., Vella, S.,Yeni, P.G.,and Volberding, P.A. Antiretroviral therapy for HIV infection in 1998. Updated recommendations of the International AIDS Society-USA Panel. JAMA 280(1):78–86

Chakraborty, H., Newman, J.E., Woelk, G., Hemingway-Foday, J., Iriondo-Perez, J., Akam, W., et al. 2011. *Antiretroviral therapy initiation and CD4 progression over time among HIV infected adults in Central Africa. International Journal of Medicine and Public Health 1 (4):3-11*

CDC's Approach to Reducing HIV Infections in the United States. 2011. High-Impact HIV Prevention

CDC HIV Surveillance Report, 2010. Volume 22. Diagnoses of HIV Infection and AIDS in the United States and Dependent Areas

CDC HIV Surveillance—United States 2011. MMWR 60(21):689–693.

CDC Report Estimated lifetime risk for diagnosis of HIV infection among Hispanics / Latinos—37 states and Puerto Rico 2010. MMWR 59(40):1297–1301.

Ezekiel, K. 2003. HIV and AIDS in Africa: Beyond Epidemiology. Blackwell Publishers ISBN 0631223576

Ford, C.L, Whetten K.D, Hall S.A, Kaufman J.S, Thrasher A.D. 2007. Black sexuality, social construction, and research targeting 'The Down Low' ('The DL'). *Ann Epidemiology* 17(3):209–216

Harrison, D 2009. '*An Overview of Health and Health care in South Africa 1994-2010: Priorities, Progress and Prospects for New Gains*' Commissioned by the Henry J. Kaiser Family Foundation

Hunter, S. 2006. AIDS in America Macmillan Publishers ISBN 9781403971999

Heron M. *Deaths: Leading Causes for 2007.* National Vital Stat Rep; Vol. 59, No. 8. Hyattsville, MD: National Center for Health Statistics; 2011

Lloyd, S.W., Ferguson, Y.O., Corbie-Smith, G., Ellison, A., Blumenthal, C., Council, B.J., et al. 2012. *The Role of Public Schools in HIV Prevention: Perspectives from African Americans in the Rural South. AIDS Education and Prevention,* 24 (1):41-53.

Muula, S.A. 2008. HIV Infection and AIDS Among Young Women in South Africa Croat Med J. June; 49(3): 423–435.

Prejean J, Song R, Hernandez A, Ziebell R, Green T, Walker F, et al 2011. *Estimated HIV incidence in the United States, 2006–2009. PLoS ONE* 20 6(8):1–13

Salim, K. 2005. HIV/AIDS in South Africa Cambridge University press ISBN: 9780521616294

VIII. Special Resource Requirements

None

IX. Bibiliography

Amaro, H. 2000. "*On the margin: Power and women's HIV risk reduction strategies.*" *Sex Roles* 42(7-8): 723-749.

Bowleg, L. 2000. "*Gender roles, power strategies, and precautionary sexual self-efficacy: Implications for Black and Latina women's HIV/AIDS protective behaviors.*" *Sex Roles* 42(7-8): 613-635.

Brian G. Williams, James O.Lloyd-Smith Eleanor Gouws, Catherine Hankins, Wayne M. Getz, John Hargrove, Isabelle de Zoysa, Christopher Dye, Bertran Auvert 2011. *The Potential Impact of Male Circumcision on HIV in Sub-Saharan Africa* PLoS Medicine 3:7 1032-1040

Buck, J., M. S. Kang, et al. 2005. "*Barrier method preferences and perceptions among Zimbabwean women and their partners.*" *Aids and Behavior* 9(4): 415-422.

Campbell, C. A. 1995. "*Male Gender-Roles and Sexuality - Implications for Womens Aids Risk and Prevention.*" Social Science & Medicine 41(2): 197-210.

Cellucci, L.W. & Celluci, T. 1998. *HIV disease and the elderly: Coming of age in the era of AIDS.* In *Social gerontology*, David E. Redburn & Robert P. McNamara, eds., pp.93-114. Westport, CT: Auburn House.

Frankenberg, R., P. Aggleton, et al. 1989. *One epidemic or three: Cultural, social and historical aspects of the AIDS pandemic.* Oxford, England, Falmer Press/Taylor & Francis, Inc. viii, 276 pp.

Freeman, A., Newman, J., Hemingway-Foday, J., Iriondo-Perez, J., Stolka, K., Akam, W., Balimba, A., Kalenga, L., Mbaya, M., Mfangam, M.B., Mukumbi, H., Niyongabo, T., Woelk, G., et al. 2012 *Comparison of HIV-positive women with children and without children accessing HIV care and treatment in the IeDEA Central Africa cohort.* *AIDS Care*, 24 (6):673-679.

Gollub, E. L. 2000. "*The female condom: Tool for women's empowerment.*" *American Journal of Public Health* 90(9): 1377-1381.

Klitzman,R. 1997. *Being Positive: The Lives of Men and Women With HIV* ISBN 1-56663-164-5; Ivan R. Dee, Publisher, 15200 NBN Way, Blue Ridge Summit, PA

Lewis, M. G. 2003. *AIDS: Women, men, empowerment, mobilization*, VSO - Voluntary Service Overseas (UK), London, 53 pp

Myrick, R. 1996. *AIDS, Communication and Empowerment: Gay Male Identity and the Politics of Public Health Messages* ISBN: 1-56023-884-4; The Haworth Press, Inc.,

Nazeema, A., Alan j., Catherine, F., Wanjiru M., and Shahieda J. 2009. *HIV education in South African schools: The dilemma and conflicts of educators Scandinavian* Journal of Public Health 37(Suppl 2): 48–54

Nichols, J.E., Speer, D.C. Watson, B. J. et al 2002. *Aging with HIV: Psychosocial, Social, and Health Issues.* San Diego: Academic Press, Inc.

Ober, A.J., Iguchi, M.Y., Weiss, R.E., Gorbach, P.M., Heimer, R., Ouellet, L.J., Shoptaw, S., Anglin, M.D., Zule, W.A. 2011. *The Relative Role of Perceived Partner Risks in Promoting Condom Use in a Three-City Sample of High-Risk, Low-Income Women. AIDS and Behavior*, 15 (7):1347-1358.

Pettifor, A. E., D. M. Measham, et al. 2004. "*Sexual power and HIV risk, South Africa.*" Emerg Infect Dis 10(11): 1996-2004.

Richter, L. 2004. The impact of HIV/AIDS on the development of children. In Pharoah, R. (Ed.) *A generation at risk: HIV/AIDS, vulnerable children and security on Southern Africa.* Pretoria, Institute of Security Studies.

Shaeffer, S. 1994. The Impact of HIV/AIDS on Education. *A Review of Literature and Experience.Paris, UNESCO.* Document available online

Shelley, G., Janice G., and Warren A., 1995. *Forgotten Children of the AIDS Epidemic* Yale University Press

Shetty, A. K. & PowelL, G. 2003. *Children orphaned by AIDS: A global perspective. Seminars in Pediatric Infectious Diseases,* 14, 25-31.

Stillwater, E. 2006. *AIDS and the Ecology of Poverty*, Oxford University Press.

Suzanne L. G. 2006 *The Greater Involvement of People Living with and Affected by HIV and AIDS (GIPA): NGO Experiences and Implications for the Work of Oxfam International and Oxfam Australia*, July 2006, 50 pp.

UNAIDS 2006. Report on the Global AIDS Epidemic. New York, UNAIDS. Document available online

UNICEF 2007.Caring for Children affected by HIV and AIDS. Florence, UNICEF. Document available online

Visser, M. J., Schoeman, J. B. & Perold, J. J. 2004. Evaluation of HIV/AIDS prevention in South African schools. *Journal of Health Psychology,* 9, 263-280.

Wolf, B. 1996. *HIV Positive.* ISBN: 0-925190-99-3 The Haworth Press

Online Syllabus

BIOL 117 Understanding HIV Biology and AIDS

Dr. Narayanaswamy Bharathan 213 Weyandt Hall

724-357-2584 bharathn@iup.edu

Online Office Hours: *[Hours to be added when course is taught]**

On-Campus Office Hours: *[Hours to be added when course is taught]**
During online office hours, I am available by telephone and e-mail and other means of communication by special arrangement. If you are unable to make online office hours, other times can be arranged by appointment. For on-campus office hours, you can stop by or contact me via telephone. Other on-campus times are also available by appointment.

*All times presented in the course syllabus and schedules are expressed in Eastern Time (ET).

Course Catalog Description

BIOL 117 Understanding HIV Biology and AIDS 3c-0l-3cr

Prerequisites: Non-Biology department majors and minors only

An introduction to the mode of infection and prevention of AIDS virus which are used as an illustration of biological principles. Profiles biological indicators for HIV disease and its progression to AIDS. Therapeutic and non-therapeutic approaches to treat HIV infections are emphasized. (Does not count toward Biology Electives, Controlled Electives, or Ancillary Sciences for Biology majors and minors.)

Course Objectives

Course Outcomes and Assessment (Expected Undergraduate Student Learning Outcomes – EUSLO)

Objective 1:

Describe the general characteristics of HIV transmission as a means to interpret the Biology of virus.

Expected Student Learning Outcomes 1 and 2:

Informed and Empowered Learners

Rationale:

Assignments will require students to have a level of knowledge of circulatory system and immunology that will enable them to understand how these systems work. Assignments will also require students to critically analyze immune systems modalities and to use this analysis to explain how HIV testing is interpreted.

Objective 2:

Compare how general virus transmission has been perceived throughout the ages by identifying the common and uncommon modes of transmission of the HIV and AIDS.

Expected Student Learning Outcome 2:

Empowered Learners

Rationale:

Assignments will require students to evaluate common modes of virus transmission (air-borne, water, vector and non-vector, and blood). In addition, these assignments will engage students in assessing a knowledge base in science and how that knowledge influenced the perception and treatment of individuals infected with HIV.

Objective 3:

Describe how HIV infection and AIDS is perceived and dealt with in today's society.

Expected Student Learning Outcome 3:

Responsible Learners

Rationale:

Assignments will require students to assess their own views of HIV and AIDS infection and how they compare to ethical judgments and social responsibilities in various societies around the world. They will also explore how their personal actions and civic values influence their perception of people having AIDS. Other assignments will have the students analyze AIDS issues in the public realm (e.g., national, state, or local) and to use this analysis to determine how their personal lives are and will be affected.

Objective 4:

Assess historical figures in last 40 years who have made contributions to our understanding of HIV and AIDS.

Expected Student Learning Outcome 1 and 2:

Informed and Empowered Learners

Rationale:

Assignments will require students to gain an understanding of how we have arrived at our current understanding of HIV transmission and prevention by analyzing the distribution of HIV among individuals and populations throughout last three decades. They will then apply these analyses to the evaluation of their own view of HIV transmission and prevention.

Required Textbook

You must purchase the following texts and materials to successfully complete this course:

- Gerald J. J. Stine. 2012. *AIDS Update: An annual Overview of Acquired Immune Deficiency syndrome.* ISBN13: 9780073527659 McGraw Hill Publishers available at the IUP Co-op Store 1-800-537-7916, co-opstore@iup.edu. (Note: The Co-op Store may have used books that are the correct edition, and they will mail the books to you.
- This course will make use of several videos for online viewing. Viewing these videos will require access to a broadband connection (DSL, Cable, High-Speed Internet). While most of the course can be completed on a low-bandwidth connection, such as dial-up, it is recommended that you obtain broadband access or find a location from which you can access a broadband connection.
- Additional supplemental non-text book reading materials will be provided through IUP's learning management system.

Supplemental Non-Textbook Reading

Barnett, T., and Whiteside, A., 2006. *AIDS in the Twenty-First Century: Disease and Globalization.* ISBN10: 1403997683. Palgrave **Publishers**

Hung, F., Conner, R., and Villarreal, L., 2012. *AIDS Science and Society* ISBN 0-7637-0086. Bartlett Publishers

Shelby, R.D., Aronstein, D.M. and Thompson, B.J., 1998. *HIV And Social Work: A Practitioner's Guide (Psychosocial Issues of HIV/AIDS)* ISBN10: 1560239069. Haworth Press, Inc.

Suggested Readings

Carpenter, C.C., Fischl, M.A.,Hammer, S.M., Hirsch, M.S., Jacobsen, D.M., Katzenstein, D.A., Montaner, J.S., Richman, D.D., Saag, M.S., Schooley, R.T.,Thompson, M.A., Vella, S.,Yeni, P.G.,and Volberding, P.A. Antiretroviral therapy for HIV infection in 1998. Updated recommendations of the International AIDS Society-USA Panel. JAMA 280(1):78–86

Chakraborty, H., Newman, J.E., Woelk, G., Hemingway-Foday, J., Iriondo-Perez, J., Akam, W., et al. 2011. *Antiretroviral therapy initiation and CD4 progression over time among HIV infected adults in Central Africa. International Journal of Medicine and Public Health 1 (4):3-11*

CDC's Approach to Reducing HIV Infections in the United States. 2011. High-Impact HIV Prevention

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Required Technology Skills and Software Technology Skills
Students enrolled in this course should possess the following technology skills:

- The ability to access information via the Web
- The ability to use The learning management system and associated tools, including discussion/chat, quizzing, and assignment submission features
- The ability to use word processing software and to save in the appropriate format
- The ability to use Internet communication tools, specifically the IUP e-mail system (iMail)
- The ability to attach files on email message
- The ability to demonstrate netiquette (appropriate online conduct)

Software
The following software is required in order to view course content and to participate in planned course activities. If you do not have this software currently loaded on your computer or are unsure, you can download the software for free by clicking on the following links:

- Adobe Reader (http://get.adobe.com/reader/)
- Flash Player (http://get.adobe.com/flashplayer/)
- Window Media Player

You will need an office productivity suite, such as Microsoft Office or Open Office (available free at http:www.openoffice.org). You will be required to turn in word processed assignments and to work with electronic software at various points in the semester.

Technical Support
To obtain technical support for computer issues related to this course, please contact Indiana University of Pennsylvania's IT Support Center Monday-Friday between 7:30am-5:30pm Eastern Time (ET) by logging a ticket at http://ihelp.iup.edu. If you have trouble accessing this site, please call 724-357-4000. You should be prepared to give specific details regarding your technical issue(s), including what you were doing before the error occurred and the exact text of any error messages received.

After hours and weekend support for Desire2Learn can be obtained at 1-877-325-7778 or by completing D2L's Web form.

Course Participation Requirements
Course modules will be assigned on a weekly basis according to the Course Schedule and include objectives, lesson guide, and expectations for completing homework assignments. You are expected to actively participate in all aspects of the course. This

includes completion of assigned readings, homework assignments, self-tests and exams and participation in online discussions. By design, you will be expected to participate in the course daily. Course modules have definitive timeframes, and grades for discussion posts and assessments are assigned after every module. All work assigned in course modules(s) must be turned in by the end of the course week unless otherwise noted. **Late work will not be accepted.** It is suggested that you read through all course content in the week's assigned module(s) to get a feel for what is expected during the course week and to help you plan your time wisely.

For any forum discussions in the course, you must have a minimum of one original post and two responses to other student's posts. You should also read all of the posts before responding so as to not duplicate information. For small-group discussions, the instructor will be assigning a student to serve as the group discussion leader. This means prior to the small-group discussion, you will want to prepare your discussion items so that you are ready and can post to the discussion board as close to the beginning of the module as possible.

E-mail
IUP e-mail (i-Mail) is the official means of communication of the University. You should be sure to check your e-mail daily. Important class announcements will be sent to your IUP e-mail account.

Questions Regarding the Course or Course Content
It is understood that questions about the course and the course content will come up from time to time. If you have a question for the instructor, please do the following:

- Post a message to the Course Questions discussion forum—This forum is located in the course's introductory module. If you have a question about the course, other students may also have the same question as you. Posting your question here enables the instructor to respond to your question, as well as to assist other students in the course who may have the same question.
- Contact the Instructor directly—The Course Questions discussion forum may not be the appropriate place to ask certain questions, such as questions regarding personal matters and individual course grades. You may also contact the instructor via e-mail or telephone with your questions.

Online Discussions (Forums)
Throughout the course, you will participate in a series of small-group discussions. The instructor will be assigning students to serve as the weekly discussion leaders in each group. Prior to your assigned discussion you will want to prepare your discussion items so that you are ready and can post to the discussion boards as close to the beginning date of the discussion a possible.

As discussion leaders and/or participants in the discussions, you must make at least one original post and a minimum of two responses to other students' posts for each discussion. You are also expected to read all postings as part of the discussion.

Discussion forums will be graded following the discussion deadline noted in the Course Schedule. Your participation in the discussion forums will be evaluated according to the Group Discussion Rubric. Posts made after the due date will not be graded, resulting in a loss of points toward your final grade. It is imperative that you follow the discussion forums, as many questions and issues regarding the course content will be answered through these forums.

Online Etiquette
Discussion, chat, and e-mail spaces within this course are for class purposes only, unless otherwise stated. Please remember to conduct yourself collegially and professionally. Unlike in the classroom setting, what you say in the online environment is documented and not easily erased of forgotten. The following guidelines:

- Avoid using ALL CAPS, sarcasm, and language that could come across as strong or offensive.
- Read all postings before posting your responses to discussion topics so as to not repeat information.
- Keep chat comments brief and to the point. Use /// to indicate that you are finished sharing your input.
- Focus on one topic at a time when chatting or posting to discussions.
- Remember that unlike in face-to-face learning environments what you say in discussions and chats is documented and available to be revisited. Choose your words and discussion topics carefully.
- Course e-mail should only be used for messages pertaining to the course. Please refrain from sending forwards, jokes, etc. within e-mail.
- When posting, make sure to check grammar and spelling before submitting your post.

Students with Disabilities
If you are a student who has a documented disability and need special accommodations, the instructor will work with you to provide reasonable accommodation to ensure you a fair opportunity to perform in the class. Please advise the instructor in the first week of the semester regarding the disability and the desired accommodations. Assistance for individuals with disabilities is available through IUP Disability Support Services at http://www.iup.edu/disabilitysupport or at 724-357-4067.

Academic Integrity Policy

Indiana University of Pennsylvania expects a full commitment to academic integrity from each student. This syllabus represents a contract between you and the instructor of this course and that you agree to follow the rules and expectations set up therein. Academic integrity means

- Providing or receiving unauthorized assistance in coursework, including papers, quizzes, and examinations.
- Using unauthorized materials and resources during quizzes and tests.
- Possessing course examination materials without the prior knowledge of the instructor.
- Plagiarizing, using papers, dissertations, essays, reports, speeches, and oral presentations, take-home examinations, computer projects, and other academic exercises or passing off of ideas or facts beyond common knowledge, without attribution to their originators.
- Engaging in behaviors that are disruptive or threatening to others.
- Using computer technology in any way other than for the purposes intended for the course.

Please note that the IUP faculty uses a variety of technologies to check the authenticity of student work. Violations of academic integrity will be handled per IUP's Academic Integrity Policy and Procedures. Failure to comply with the policies and procedures may result in a decrease in grade, involuntary withdrawal from an academic program, suspension, expulsion, or rescission of a conferred degree. IUP's full policy on academic integrity is available in the Undergraduate Catalog under Academic Policies at http://www.iup.edu/registrar/catalog.

Evaluation Methods

1. Final Exam (15%)—you will be required to take a final comprehensive exam on the course content. The exam will consist of multiple choice questions. The exam will take place on the last day of class, and you will only have one attempt.

2. Self-Tests (30%; 5% for each case study)—you will be given six multiple-choice self-tests that relate to the material from your readings and the online resources. Self-tests are designed to assess your understanding of the material and to provide you feedback. You will be evaluated on your ability to correctly respond to the questions. You may take each self-test two times, and must score at least 60% to move on to the next module. If you do not meet the minimum score, you should seek consultation with instructor.

3. Case Studies (20%; 10% for each case study)—you will be assigned two case studies. These case studies will cover the global impacts of HIV/AIDS, role of anti-retroviral therapies and their opportunities and challenges, the prevention among minority communities, and the risk factors generally associated with HIV transmission. You must prepare a response to each case study based on the questions provided by the instructor.

You will be evaluated on the case studies based on their ability to summarize the case, respond to questions, and provide support using textbook and online resources.

4. Forum Discussions (25%; 5% for each discussion)—You will be assigned to participate in five small-group, student-led forum discussions throughout the semester. These discussions will cover course resources and materials regarding topics, such as transmission, stigmatization, legal issues, and models of AIDS management. For each discussion, the student leader will facilitate the discussion, in consultation with the instructor, regarding the assigned readings and materials. Students will be evaluated on their posting quality, posting frequency, and grammar and spelling as outlined in the Group Discussion Rubric.

5. Critique of Non-Textbook Reading (10%)—You may select one of the supplemental texts for the course to read and write a critique. Critique papers should be a minimum of five pages and demonstrate a connection to the course content, quality of the response, use of technical and descriptive terms associated with HIV/AIDS, and grammar and spelling.

Grading

The following grading scale will be used: A: 90-100%; B: 80-89%; C: 70-79%; D: 60-69%; F: below 60%

Grading Policies

Incomplete grades

Incomplete grades will only be granted in the event of major life crisis. The instructor reserves the right of judgment as to what qualifies as a major life crisis.

Withdrawal Grades

According to IUP Policy, if you wish to receive a withdrawal (W) grades for the course, you must do so by university deadline for processing withdrawals, which can be found on the IUP URSA page in the academic calendar. A student who fails to withdraw by the deadline must file for a deadline waiver through the dean of his or her college and provide documentation of catastrophic circumstances preventing the student from completing the course/semester. In the event withdrawal would be required, failure to process a withdrawal will result in a failing grade for the course.

Course Schedule

Each module will cover several types of assessments. Weekly activities may include review of chapters, self-tests, case studies, and forum discussions based on assigned readings, slide presentations, supplemental readings.

Module 1 (Week 1)
Introduction to BIOL 117

1. Review the Course Overview.
2. Review of the Syllabus and Course Policies.
3. Post an introduction to the class.

Module 2 (Week 2)
Characteristics of Viruses, Infectious Diseases, and the Pandemic Nature of AIDS

1. Connect to the book's website: http://biology.jbpub.com/fan/aids/7e/
2. Read textbook Chapters 1 and 2.
3. D2L content Introduction to HIV and AIDS:
   a. General Characteristics of Viruses
   b. Why AIDS is a Syndrome and Not a Disease
   c. Factors that Affect the Spread of Epidemics
   d. Koch's Postulates
   e. Differentiate Between Chronic and Acute Infections
   f. Epidemic, Endemic, and Pandemic Nature of HIV and AIDS
   g. Orgin of HIV
4. Answer review questions for these Chapters 1 & 2 to assist you in preparing for the self-test.
5. Play the Avert Challenge game http://www.avert.org/avert-aids-challenge.htm
6. Origin of HIV and Transmission to Humans
   a. Watch Video: http://topdocumentaryfilms.com/origins-aids/
   b. Read: http://www.avert.org/origin-aids-hiv.htm
7. **Due:** Forum Discussion #1: The Origin of HIV
8. **Due:** Self-Test #1

Module 3 (Week 3)
Immune System

1. Read textbook Chapter 3.
2. D2L Content
   a. Blood
   b. Innate Immunity
   c. Adaptive Immunity
   d. Humoral Immunity
   e. T-Cells and Cell-Mediated Immunity
3. Read: http://aids.gov/hiv-aids-basics/just-diagnosed-with-hiv-aids/hiv-in-your-body/immune-system-101/index.html
4. Read article http://www.niaid.nih.gov/topics/hivaids/understanding/biology/Pages/devastatesImmuneSystem.aspx
5. **Due:** Forum Discussion # 2: How HIV Devastates the Immune System

Module 4 (Week 4)
Biology of HIV

1. Read textbook Chapter 4.
2. D2L Content
   a. Life Cycle of Retrovirus
   b. Features of HIV
   c. Nature of the HIV receptor
   d. Effects of HIV infections on Individuals

3. Read : http://aidsinfo.nih.gov/contentfiles/HIVAIDS_theBasics.pdf
4. Read: http://aidsinfo.nih.gov/contentfiles/HIVLifeCycle_FS_en.pdf
5. Watch Video: http://highered.mcgraw-hill.com/sites/0072495855/student_view0/chapter24/animation__how_the_hiv_infection_cycle_works.html
6. **Due:** Case Study #1 Read article http://www.publichealthreports.org/issueopen.cfm?articleID=2031 Answer questions

Module 5 (Week 5)
Biological Indicators for HIV Disease and Progression to AIDS

1. Read textbook Chapter 5.
2. D2L Content
   a. Exposure Versus Infection
   b. HIV Infection in Untreated Individuals
   c. Primary Infection and Asymptomatic Period
   d. Damage to the Immune System and Full Blown AIDS
   e. High Turnover of T-Cells
3. Read "Stages of HIV Infection" and "What Does HIV Do When It is Not Treated?": **http://aids.gov/hiv-aids-basics/just-diagnosed-with-hiv-aids/hiv-in-your-body/stages-of-hiv/index.html**
4. Read "Clinical Progression of HIV": **http://www.niaid.nih.gov/topics/HIVAIDS/Understanding/Biology/pages/clinicalcourse.aspx**
5. **Due:** Self-Test #2

Module 6 (Week 6)
HIV Transmission

1. Read textbook Chapter 7.
2. D2L Content
   a. Biological Bases of HIV transmission
   b. Sources of Infectious HIV
   c. Stability of HIV in Blood
   d. Activities Not Associated with Transmission
   e. Activities Associated with HIV Transmission: Birth, Blood, and Sex
3. Read: http://www.niaid.nih.gov/topics/HIVAIDS/Understanding/Pages/riskFactors.aspx
4. Read:
   a. Mother-to-Child Transmission of HIV: http://aidsinfo.nih.gov/contentfiles/Mother-to-ChildTransmissionofHIV_FS_en.pdf
   b. HIV Testing and Pregnancy http://aidsinfo.nih.gov/contentfiles/HIVTestingandPregnancy_FS_en.pdf
   c. Safety of Anti-HIV Medications During Pregnancy http://aidsinfo.nih.gov/contentfiles/SafetyandToxicityofAntiHIVMedsDuringPregnancy_FS_en.pdf
5. **Due:** Forum Discussion # 3 HIV Mother-to-Child Transmission

Module 7 (Week 7)
Transmission Prevention

1. Read textbook Chapter 9.
2. D2L Content
   a. Principles of Quarantine
   b. Disease Prevention and Health Promotion in Schools
   c. Models of Health Behavior Change
   d. Examples of HIV/AIDS Prevention Programs
3. Read: http://www.avert.org/aids-hiv-prevention.htm
4. **Due:** Forum Discussion #4: Blood safety
   a. Blood Donations, Transfusions, and HIV
   b. Medical Injections and HIV
   c. Occupational Exposure and HIV

Module 8 (Week 8)
Diagnosis of HIV and Testing

1. Read textbook Chapter 4.
2. D2L Content
   a. Direct Examination
   b. Indirect Examination (Virus Isolation)
   c. Serology
   d. Direct Genome Test
3. Read: http://www.cdc.gov/hiv/topics/testing/rapid/index.htm
4. **Due:** Forum Discussion #5: Rapid HIV testing
   a. Counseling
   b. Issues Related to Rapid HIV Testing of Women in Labor & Delivery
   c. Rapid HIV Testing Training

Module 9 (Week 9)
Therapy for HIV Disease

1. Read textbook Chapters 10 and 12.
2. D2L Content
   a. Biomedical Efforts
   b. Prevention of Infection
   c. Drug Treatments
   d. Vaccine
3. Read: About the HIV Treatment Guidelines
   http://aidsinfo.nih.gov/contentfiles/AboutHIVTreatmentGuidelines_FS_en.pdf
4. **Due:** Forum Discussion #6
   a. HIV and Vaccine
   b. HIV and AIDS Care
   c. Highly Active Antiretroviral Therapy (HAART)

Module 10 (Week 10)
Global Prevalence of HIV Infection and AIDS Cases

1. Read textbook Chapter 6.
2. D2L Content
   a. Overview of Epidemiology of AIDS in the United States
   b. AIDS Around the World
   c. AIDS in Africa
   d. AIDS in Asia
   e. HIV Subgroups
   f. Epidemiology and Modes of HIV Transmission
3. **Due:** Self-Test # 3

Project Module (Week 10)
Case Study #2

1. Case Study #2: Read and respond to the questions for HIV/AIDS: nutritional implications and impact on human development Proceedings of the Nutrition Society (2008), 67, 109–113 Answer questions http://dx.doi.org/10.1017/S0029665108006095
2. **Due:** Case Study #2

Module 11 (Week 11)
HIV Therapy and HAART

1. Read textbook Chapter 6.
2. D2L Content
   a. Principles of HIV Therapy
   b. Goals of Antiretroviral Therapy
   c. Who Should be Treated
   d. Approved Classes of Drugs in the HAART Regimens
   e. Read about the HHS Antiretroviral Therapy Guidelines: http://www.thebodypro.com/index/treat/guidelines_adult.html#guidelines

Module 12 (week 12)
Significance of HAART

1. Read textbook Chapter 5.
2. D2L Content
   a. Know the factors affecting decision on when to initiate therapy
   b. Identify the type of HAART drug currently available for treatment
   c. Compare CD4 progression with and without HAART
   d. Explain the significance of HAART and prevalence of opportunistic Infections
   e. Evaluate the role of HAART to create a perfect world without HIV and AIDS
3. Read Antiretroviral Therapy as Prevention of HIV and TB: http://whqlibdoc.who.int/hq/2012/WHO_HIV_2012.12_eng.pdf
4. **Due:** Self-Test #4

Module 13 (Week 13)
Global Strategy to Combat the Spread of HIV and AIDS

1. Read Chapters 5, 9, 10, and 12.
2. D2L Content
   Future Directions of Social Efforts (Chapter 12)
   AIDS Prevention Strategies- Chapters 5, 9, and 10)
5. **Due:** Self-Test #5

Module14 (Week 14)
Current Studies and Models of HIV Management

1. Read Chapters 5, 9, 10, and 12.
2. D2L Content
   a. Role of National Governments and United Nations efforts through WHO to combat global spread.
   b. Re-evaluation of distribution of AIDS in a global society
   c. Multidisciplinary approaches—to prevent spread
   d. Confronting the news of infection
   e. CDC current guidelines: Discussion of selected papers from the CDC *HIV/AIDS Prevention among Hispanic/Latino Communities: colloquium "The* DC's Hispanic/Latino Consultation, April 1-2, 2008"
3. **Due:** Self-Test #6

Project Module (Week 14)
Critique of Non-textbook Reading

1. Critiquing non-textbook reading and instructions.
2. Due: Non-textbook reading. Students will submit a critique with a maximum of five printed pages (10%)

Final Exam Module (Week 15)
Final Exam
Exam

1. **Due:** Final Exam [Specific date for the exam to be added when the course is taught].

Article Critique/Peer Review Rubric

Criteria	Excellent 3 Points	Good 2 Points	Acceptable 1 Point	Unacceptable 0 Points
Summary of Article	Summary written in proper paragraph format. Complete sentences, correct spelling, punctuation, & grammar, were used.	Most of Summary written in proper paragraph format. 3 to 5 errors: sentences structure, spelling, punctuation, & grammar.	Summary is incomplete missing major point and not written in an appropriate format, 6 to 10 errors: sentences structure, spelling, punctuation, & grammar.	No Summary provided or Summary is short and includes none of the major points, more than 10 errors: sentences structure, spelling, punctuation, & grammar.
Answer to Questions	All questions are answered and include explanation, rationale, and uses sources outside of book and PowerPoint.	All questions are answered and include a weak explanation, rationale, and uses sources outside of book and PowerPoint.	1 to 2 questions are not answered and include a very weak explanation, rationale, and uses no sources outside of book and PowerPoint.	Answers to questions are not provided or no explanation given for answers, and uses only book and PowerPoint resources.
Timeliness of responses	Responds to questions on time.	Occasionally responses are late.	Half the time responses are late.	Responses are often past the due date.
Comprehension of Articles	Responses summarize important points and reference specific points; responses reveal understanding, interpretation, and perspective.	Responses generally summarizes article but do not make interference to different perspectives.	Limited evidence that article was understood; superficial explanation or description of reading.	No evidence that article was even read.
Response to other students' statements	Often responds to other students statements by embellishing or disagreeing with specific explanations.	Often responds to other students statements, always agreeing.	Occasionally responds to other students.	Doesn't respond to other students.
Connections	Good connection between readings and either classroom or personal experiences.	Some connection between readings and own experiences.	Little connection between readings and experiences.	No connection between readings or experiences.

Group Discussion Rubric

Category	1 Points	2 Points	3 Points
Posting Frequency	Student made one post to the discussion board to either a topic question or a peer.	Student made two posts to the discussion board to a topic question of a peer.	Student made at least one post to the topic question and responded to at least two peers.
Content Represent significant contribution to discussion	Student makes a minimal contribution to the discussion and/or does not support the post with evidence from the course topics, materials, and resources.	Student makes postings that significantly contribute to the discussion, but does not support the post with evidence from the course topics, materials, and resources.	Student makes postings that significantly contribute to the discussion and connects post content to course topics, readings, and resources
Grammar and Spelling	Student posts contained more than 3 spelling or grammar errors.	Student posts contained 1 or 2 spelling or grammar errors.	Student posts did not contain spelling or grammar errors.

Sample Module Materials

Module 2 (Week 2)
Characteristics of Viruses, Infectious Diseases, and the Pandemic Nature of AIDS

9. Connect to the book's website: http://biology.jbpub.com/fan/aids/7e/
10. Read textbook Chapters 1 and 2.
11. D2L content Introduction to HIV and AIDS:
    h. General Characteristics of Viruses
    i. Why AIDS is a Syndrome and Not a Disease
    j. Factors that Affect the Spread of Epidemics
    k. Koch's Postulates
    l. Differentiate Between Chronic and Acute Infections
    m. Epidemic, Endemic, and Pandemic Nature of HIV and AIDS
    n. Origin of HIV
12. Answer review questions for these Chapters 1 & 2 to assist you in preparing for the self-test.
13. Play the Avert Challenge game http://www.avert.org/avert-aids-challenge.htm
14. Origin of HIV and Transmission to Humans
    a. Read: http://rstb.royalsocietypublishing.org/content/365/1552/2487.full
    b. Watch Video: http://topdocumentaryfilms.com/origins-aids/
    c. Read: http://www.avert.org/origin-aids-hiv.htm
15. **Due:** Forum Discussion #1: The Origin of HIV
16. **Due:** Self-Test #1

Small-Group Forum Discussion: Understanding HIV and AIDS

Read "The evolution of HIV-1 and the origin of AIDS" article. The article and the other resources presented in this module will assist you developing your response to the discussion questions that follow.

The evolution of HIV-1 and the origin of AIDS

Paul M. Sharp[1,*] and Beatrice H. Hahn[2,3]

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The major cause of acquired immune deficiency syndrome (AIDS) is human immunodeficiency virus type 1 (HIV-1). We have been using evolutionary comparisons to trace (i) the origin(s) of HIV-1 and (ii) the origin(s) of AIDS. The closest relatives of HIV-1 are simian immunodeficiency viruses (SIVs) infecting wild-living chimpanzees (*Pan troglodytes troglodytes*) and gorillas (*Gorilla gorilla gorilla*) in west central Africa. Phylogenetic analyses have revealed the origins of HIV-1: chimpanzees were the original hosts of this clade of viruses; four lineages of HIV-1 have arisen by independent cross-species transmissions to humans and one or two of those transmissions may have been via gorillas. However, SIVs are primarily monkey viruses: more than 40 species of African monkeys are infected with their own, species-specific, SIV and in at least some host species, the infection seems non-pathogenic. Chimpanzees acquired from monkeys two distinct forms of SIVs that recombined to produce a virus with a unique genome structure. We have found that SIV infection causes $CD4^+$ T-cell depletion and increases mortality in wild chimpanzees, and so the origin of AIDS is more ancient than the origin of HIV-1. Tracing the genetic changes that occurred as monkey viruses adapted to infect first chimpanzees and then humans may provide insights into the causes of the pathogenicity of these viruses.

Keywords: human immunodeficiency virus type 1; simian immunodeficiency virus; chimpanzee; gorilla; adaptation; tetherin

1. INTRODUCTION

The acquired immune deficiency syndrome (AIDS) was first formally recognized in patients in the USA in 1981. Subsequent characterization of the principal causative agent, human immunodeficiency virus type 1 (HIV-1), revealed that it was a retrovirus. As strains of HIV-1 were sampled from around the world, it became apparent that they exhibit extremely high genetic heterogeneity and that analysis of the evolution of this diversity can reveal insights into the prehistory of the virus (Sharp *et al.* 2001). HIV-1 strains can be divided into three distinct groups, which have very different prevalences. Groups N and O are rare, and largely restricted to Cameroon and surrounding countries. The vast majority (perhaps 98%) of HIV infections worldwide are caused by HIV-1 group M. Even within group M, there is very high diversity and the epicentre of that diversity is in Africa and in particular Kinshasa in the Democratic Republic of Congo (Vidal *et al.* 2000). While HIV-1 has an extremely fast rate of evolution, the virus must have circulated within human populations for many years before it was first recognized for this extent of diversity to have accumulated. Using molecular clocks, the common ancestor of HIV-1 group M strains has been dated to around the 1920s (Korber *et al.* 2000; Worobey *et al.* 2008). Partial characterization (Zhu *et al.* 1998; Worobey *et al.* 2008) of two viruses from samples initially obtained around 1960 in Kinshasa (then called Leopoldville) has shown that HIV-1 group M had already diversified substantially by that time, corroborating this time scale, and pointing to the location of the early diversification of these viruses (Sharp & Hahn 2008).

At the time when HIV-1 was first described, the closest known relative was visna, a virus from sheep that is the prototypic member of the genus Lentivirus. Additional lentiviruses were soon found in other primates, and a second virus (HIV-2) was found infecting humans. The viruses from non-human primates were termed simian immunodeficiency viruses (SIVs). Among the first species to be found to be naturally infected were African green monkeys (*Chlorocebus* species), where the prevalence of infection is high (greater than 50% of adults) and natural infections appear to be non-pathogenic. The number of different SIVs identified has increased steadily over the past 20 years. Currently, around 40 different primate species have been found to harbour SIVs, though information regarding prevalence and pathogenicity is lacking for most. So far, SIVs have only been found naturally infecting primates in sub-Saharan Africa, though the extent to which Asian or new world primates have been surveyed is unclear. Where multiple strains of SIVs have been characterized from a single species, they generally form a monophyletic clade, indicating that the great majority of

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One contribution of 18 to a Discussion Meeting Issue 'Genetics and the causes of evolution: 150 years of progress since Darwin'.

transmissions are intraspecific. The primate viruses as a whole, including HIV-1 and HIV-2, form a distinct clade within the lentiviruses, indicating that humans acquired their infections from other primates (Bailes *et al.* 2002). Phylogenetic analyses of these primate lentiviruses have provided remarkably detailed insights into the evolutionary origins of the human viruses.

2. THE ORIGINS OF HIV-1 AND HIV-2

The origin of HIV-2 was resolved first. HIV-2 was first found, and is still most common, among individuals from west Africa. In 1989, a closely related SIV was found in a monkey, the sooty mangabey (*Cercocebus atys*), whose natural range is in west Africa (Hirsch *et al.* 1989). Other examples of this virus, termed SIVsmm, were soon found in other captive sooty mangabeys, and then in individuals from the wild (Chen *et al.* 1996; Santiago *et al.* 2005). Closely related viruses found in captive macaques cause severe AIDS-like illness (Letvin *et al.* 1985), but SIV has not been found in wild macaques (which are Asian primates), and SIVsmm seems to be non-pathogenic in its natural host (Santiago *et al.* 2005; Keele *et al.* 2009). It soon became apparent that SIVsmm had been inadvertently transmitted to various macaque species in captivity (reviewed in Apetrei *et al.* 2005). In phylogenetic analyses, HIV-2 strains can be divided into various groups, which are interspersed among the SIVsmm lineages (Gao *et al.* 1992, 1994). These observations led to a rapid acceptance that sooty mangabeys were the source of HIV-2, and the interspersion of HIV-2 strains among the SIVsmm lineages implied that there had been multiple mangabey-to-human cross-species jumps (Hahn *et al.* 2000). Only two of these transmission events, leading to groups A and B, have given rise to viruses that have spread widely in the human population; six other lineages are each known only from viruses found in single individuals (Damond *et al.* 2004).

A virus closely related to HIV-1 was also first reported in 1989; this virus, SIVcpz, was found in two captive chimpanzees (*Pan troglodytes*) in Gabon (Peeters *et al.* 1989; Huet *et al.* 1990). However, for many years, chimpanzees were not accepted as the source of HIV-1 because it remained unclear whether wild chimpanzees are naturally infected with this virus. Over the next 10 years, many (probably more than a thousand) other chimpanzees were tested but only a single further example of SIVcpz was found, in a chimpanzee illegally imported to Belgium from Kinshasa (Peeters *et al.* 1992). Furthermore, this third example of SIVcpz was more divergent from the previous examples than might be expected for two viruses from a single host species (Vanden Haesevelde *et al.* 1996). Thus, it appeared that SIV was extremely rare in chimpanzees, and it seemed possible that both chimpanzees and humans had been infected from some other source(s), presumably some monkey species in central Africa.

In 1999, we found a fourth example of SIV from a chimpanzee. This ape was wild-caught and imported to the USA, but records of its geographical origin were not available. Chimpanzees have traditionally been divided into several subspecies (Groves 2001). Analyses of mitochondrial DNA (mtDNA) indicate four subspecies: western (*Pan troglodytes verus*), Nigerian (*Pan t. ellioti*), central (*P. t. troglodytes*) and eastern (*Pan t. schweinfurthii*) chimpanzees (Gagneux *et al.* 1999), which have non-overlapping ranges across western and central Africa (figure 1). (Note that *P. t. ellioti* was formerly termed *P. t. vellerosus*; Oates *et al.* 2009.) From mtDNA sequence analyses, we found that the two chimpanzees from Gabon were (as expected) *P. t. troglodytes*, as was the ape from the USA, while the other individual belonged to *P. t. schweinfurthii* (Gao *et al.* 1999). In contrast, it seemed likely that the vast majority of chimpanzees that had tested negative for SIVs were *P. t. verus*; this was subsequently confirmed (Prince *et al.* 2002; Switzer *et al.* 2005). Thus, the apparent scarcity of SIVs in chimpanzees could be explained by an absence of infection in the one subspecies that had been subject to the most testing. Indeed, two additional examples of SIVcpz from *P. t. troglodytes* were soon reported (Corbet *et al.* 2000).

The SIVcpz strains from *P. t. troglodytes* individuals formed a monophyletic cluster with all HIV-1 strains, with the single SIV from a *P. t. schweinfurthii* ape forming an outgroup. All subsequently characterized SIVcpz strains have conformed to this host subspecies-specific clustering, and this explained the unusually high level of divergence between the isolates from Gabon and Belgium. These observations implicated one particular chimpanzee subspecies, *P. t. troglodytes*, as the source of the human viruses (Gao *et al.* 1999). Since the various HIV-1 groups are interspersed among the SIVcpz lineages, each must have had a separate origin (figure 2).

Before 2002, all SIVs were isolated from blood or tissue samples. This severely limited the extent to which rare and endangered primate species could be tested for more SIV strains, and in particular prevented estimation of the prevalence of SIVs in wild chimpanzee populations. Therefore, we developed an approach for non-invasive screening of wild primates, using faecal samples; from these, we are able to detect antibodies against SIVs and obtain nucleotide sequences from both the host and the virus (Santiago *et al.* 2002). The species and subspecies, as well as the sex and identity, of the host can be established from mtDNA and various nuclear DNA markers, respectively. Using this non-invasive sampling technique, we have been able to show that SIVcpz infection is quite common and widespread among both central and eastern chimpanzees (Santiago *et al.* 2003; Worobey *et al.* 2004; Keele *et al.* 2006, 2009; Van Heuverswyn *et al.* 2007). However, the prevalence is patchy: in some areas, around one-third of individuals are infected, whereas in other areas the virus appears to be absent. These surveys have finally established that chimpanzees are indeed the natural reservoir for SIVcpz and the source of HIV-1, and have also supported the contention that *P. t. verus*, and in addition *P. t. ellioti*, are not infected with SIVs.

Initial phylogenetic analyses of the viral sequences obtained by non-invasive sampling revealed two key points (Keele *et al.* 2006). First, among the

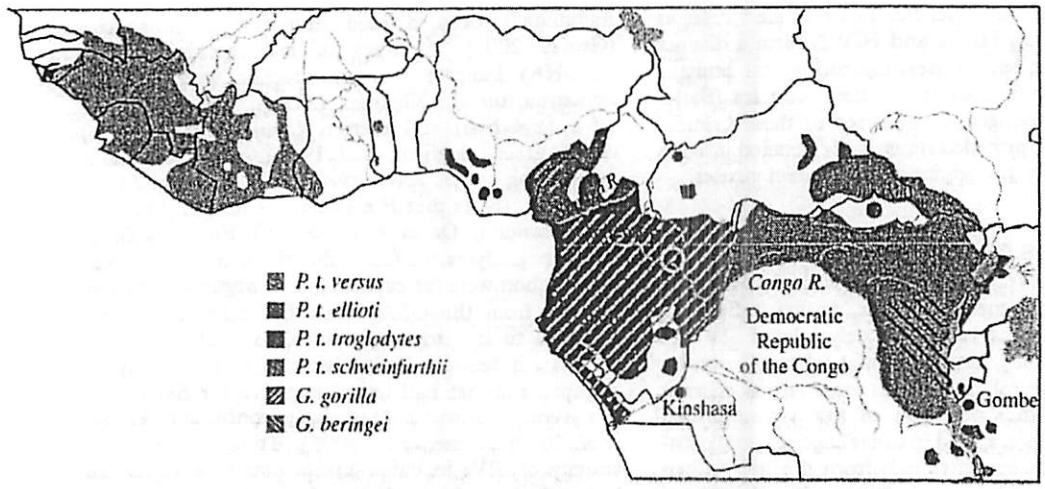

Figure 1. Map of west and central Africa, showing the ranges of chimpanzee subspecies (colour coded). The ranges of western lowland gorillas (*G. gorilla*) and eastern Grauer's gorillas (*G. beringei*) are superimposed. The gold circle denotes the region in southeast Cameroon where SIVcpz strains closely related to HIV-1 group M are found.

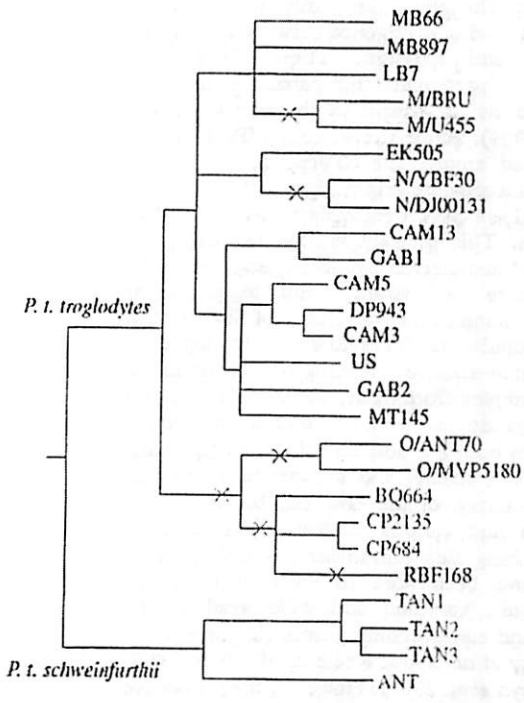

Figure 2. Origins of HIV-1. The phylogenetic relationships among strains of SIVcpz (black from *P. t. troglodytes*, grey from *P. t. schweinfurthii*), SIVgor (blue) and HIV-1 (red). The red crosses mark four branches on which cross-species jumps to humans occurred; the two blue crosses indicate alternative possible branches on which a chimpanzee-to-gorilla transmission occurred. The HIV-1 strains fall into three groups (M, N and O; only two representatives of each group are shown), and a recently described fourth lineage (RBF168). Adapted from trees shown in Takehisa *et al.* (2009) and Plantier *et al.* (2009).

newly described viruses were two clades of strains extremely closely related to HIV-1 groups M and N, respectively (figure 2). Second, the strains of SIVcpz displayed phylogeographic clustering; that is, multiple strains obtained from any one location formed monophyletic clusters, while sample sites separated by geographical barriers (typically large rivers) either were discordant with regard to the presence or absence of SIV infections, or featured strains of SIVs that were not especially closely related. This observation strongly suggests that the transmissions from chimpanzee to human that gave rise to groups M and N most probably occurred in the locations where the closely related SIVcpz strains were found. In particular, these analyses pinpoint the probable source of the viruses that gave rise to the HIV-1 group M pandemic as being chimpanzees in the extreme southeast corner of Cameroon (figure 1), in an area flanked by the Boumba, Ngoko and Sangha rivers (Keele *et al.* 2006).

While HIV-1 group O also falls within the radiation of SIVcpz strains, none of the chimpanzee viruses were particularly closely related to HIV-1 group O. Further analyses of ape faecal samples from across Cameroon revealed group O-related viruses in gorillas (*Gorilla gorilla gorilla*) (Van Heuverswyn *et al.* 2006; Takehisa *et al.* 2009). Very recently, Plantier *et al.* (2009) have reported an HIV-1 strain that does not fall within any of the three described groups, and so must represent a fourth cross-species transmission; if viruses from this lineage are found in other individuals, they will constitute a fourth group, P. This new strain of HIV-1 is very closely related to the gorilla viruses (SIVgor), and has most probably resulted from gorilla-to-human transmission. At present, it is unclear whether gorillas were also the immediate source of HIV-1 group O, or whether chimpanzee viruses were transmitted in parallel to gorillas and humans (figure 2).

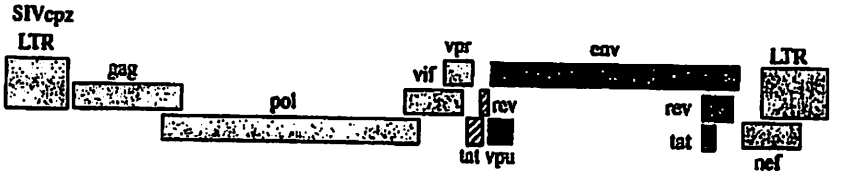

Figure 3. Mosaic structure of the SIVcpz genome. Boxes denote the long terminal repeat (LTR) regions and nine genes (*tat* and *rev* each have two exons). The SIVcpz genome arose through recombination; regions in light and dark grey were derived from the SIVrcm and SIVgsn/SIVmus/SIVmon lineages, respectively (the origin of the 5′ exons of *tat* and *rev* is difficult to determine).

3. THE ORIGIN OF AIDS

The conclusion that HIV-1 was derived from a virus infecting chimpanzees is particularly interesting, because chimpanzees and humans are so closely related. This raises a number of questions, such as the origin of the chimpanzee virus, whether adaptation of SIVcpz to infecting chimpanzees rendered the virus more capable of infecting humans and whether SIVcpz infection of chimpanzees is pathogenic.

SIVagm infections of African green monkeys and SIVsmm infections of sooty mangabeys appear to be non-pathogenic (Silvestri 2008). Extrapolating from this, it has been generally assumed that all natural SIV infections, including that of chimpanzees, are harmless. If true, the origin of AIDS coincided with the origin of HIV. However, we have recently reported evidence that contradicts this (Keele *et al.* 2009). The SIV infection status of two habituated communities of chimpanzees at Gombe National Park in Tanzania has been studied since 2001 (Santiago *et al.* 2002). From more than 550 chimpanzee-years of observations, we found that SIV infection was associated with a 10- to 16-fold increase in age-corrected risk of death. It was also found that fertility was significantly reduced in SIV-positive females, both in terms of their birth rate and the survival of their offspring. The primary symptom of AIDS in humans is a reduction in the number of $CD4^+$ T-cells; the depletion of these cells reduces host defences against secondary infections. It was possible to determine $CD4^+$ T-cell counts for five deceased chimpanzees. Tissues from three SIV-positive chimpanzees had significantly lower counts than those from two SIV-negative individuals. Two of the three SIV-positive individuals had died of trauma-related causes, while the third had no obvious injuries but displayed weakness and lethargy; this third chimpanzee had the lowest $CD4^+$ T-cell counts and tissue samples from this individual closely resembled the histopathology of human end-stage AIDS patients (Keele *et al.* 2009). While it has only so far been possible to assess the pathogenicity of SIVcpz at Gombe, where the apes are eastern chimpanzees (figure 1), there is no reason to believe that SIVcpz infection of central chimpanzees differs in any substantial way. These observations strongly suggest that SIVcpz infections in wild chimpanzees have a very similar effect to HIV-1 infections of humans.

Since most SIVs infect monkey species, whereas chimpanzees (like humans) are apes, it has always seemed likely that chimpanzees initially acquired SIVs from monkeys. However, none of the monkey SIVs described prior to 2001 were especially closely related to SIVcpz. When SIVrcm was found in red-capped mangabeys (*Cercocebus torquatus*), it was noted that the 5′ half of the genome was most similar to SIVcpz (Beer *et al.* 2001). Soon after, a virus (SIVgsn) was found in greater spot-nosed monkeys (*Cercopithecus nictitans*), where the 3′ half of the genome was most similar to SIVcpz (Courgnaud *et al.* 2002). Both SIVrcm and SIVgsn were interpreted as being recombinants between SIVcpz and other, as yet unidentified, SIV lineages. However, we showed that it is more likely that SIVcpz arose from recombination between the SIVrcm and SIVgsn lineages (Bailes *et al.* 2003), obviating the need to invoke other unknown SIVs. Subsequently, viruses (SIVmus and SIVmon) closely related to SIVgsn were found in mustached guenons (*Cercopithecus cephus*) and mona monkeys (*Cercopithecus mona*) (Courgnaud *et al.* 2003), and it can be seen that it was an ancestor of these three SIVs that was involved in the recombination event that generated SIVcpz (Sharp *et al.* 2005). Thus, it appears that chimpanzees acquired SIVs from two different species of monkeys, most probably by predation. The current ranges of red-capped mangabeys and the relevant *Cercopithecus* species overlap that of *P. t. troglodytes* in west central Africa (Groves 2001), and so it appears likely that this subspecies was first infected. The two monkey viruses then recombined, and this mosaic spread to become the only form now found in chimpanzees, and the ancestor of HIV-1 and SIVgor.

This recombinant virus has a genome structure unique among the SIVs (figure 3). First, it has a *vpu* gene overlapping the 5′ end of the *env* gene. This *vpu* gene is not present in the genomes of most monkey SIVs (including SIVrcm), but is found in viruses from the lineage including SIVgsn, SIVmus and SIVmon. Second, while in most SIV genomes there is a short overlap between the 3′ end of the *env* gene and the 5′ end of the *nef* gene, in SIVcpz there is none. This region has been duplicated in SIVcpz, presumably during the recombination event, because each of the duplicate copies was derived from a different parental virus (Schindler *et al.* 2006).

It has been found that most SIVs, and in particular those for which there is the best evidence of non-pathogenicity in the natural host (SIVsmm and SIVagm), encode a Nef protein that downregulates the T-cell receptor CD3 and thereby suppresses T-cell activation; in contrast, the Nef protein of SIVcpz, like that of HIV-1, does not downregulate CD3 (Schindler *et al.* 2006). This is surprising because the *nef* gene of SIVcpz was derived from the SIVrcm

lineage (figure 3) and SIVrcm Nef does downregulate CD3 (Schindler *et al.* 2006); thus, the Nef protein of SIVcpz has lost this activity. Since high-level immune activation is associated with progression to AIDS, this change in the properties of SIVcpz Nef correlates with pathogenicity. It is not known whether SIVgsn, SIVmus or SIVmon are pathogenic in their natural hosts. The Nef proteins of these viruses also do not downregulate CD3, but since the *nef* gene of SIVcpz was not acquired from the SIVgsn lineage, this property must have evolved independently in SIVcpz. The shared feature of the viruses that do not downregulate CD3 is the presence of a *vpu* gene, but it is not clear why this might have prompted the *nef* gene to evolve to lose this function.

4. HOST ADAPTATION

HIVs and SIVs interact with many host proteins (Bushman *et al.* 2009). Since many of those host proteins have diverged since the common ancestor of Old World monkeys and apes, it is likely that when chimpanzees first acquired SIV, the virus had to adapt in order to replicate efficiently and spread in its new host. Chimpanzees and humans are genetically very similar owing to their recent common ancestry, but there is also evidence that differences between chimpanzee and human proteins placed selection pressures on SIVcpz after it jumped from chimpanzees to humans.

Tetherin is a mammalian protein with a recently discovered antiviral activity. Tetherin dimers appear to form 'tethers' between virus envelopes and the cytoplasmic membrane of the cell, preventing the release of those viruses (Neil *et al.* 2008). The Vpu protein of HIV-1 has long been known to promote the release of progeny virions, and it is now known that this is mediated by antagonizing tetherin. However, as described above, the *vpu* gene is present in only a few SIV genomes. In SIVsmm and SIVagm, which lack *vpu* genes, the Nef protein has anti-tetherin activity (Jia *et al.* 2009; Zhang *et al.* 2009). Nevertheless, it was surprising to find that in SIVcpz, it is the Nef protein, rather than the Vpu protein, that counteracts tetherin (Sauter *et al.* 2009). When SIVcpz was formed by recombination, it acquired two genes with potential anti-tetherin activity: a *vpu* gene from the SIVgsn lineage and a *nef* gene from SIVrcm (figure 3); the Vpu protein of SIVgsn has been shown to counteract greater spot-nosed monkey tetherin (Sauter *et al.* 2009), while the Nef protein of SIVrcm is expected to function against mangabey tetherin (although this has not yet been tested experimentally). However, there is species specificity in these interactions, reflecting divergence in the tetherin sequences of different primates. Thus, when SIVs first infected chimpanzees, it is likely that neither the Vpu nor the Nef protein had full anti-tetherin activity; certainly Vpu proteins from contemporary SIVgsn, SIVmon or SIVmus strains have no activity against chimpanzee tetherin (Sauter *et al.* 2009). Vpu and Nef antagonize tetherin through interactions with different parts of the tetherin protein: for Vpu it is the transmembrane (TM) region, and for Nef the cytoplasmic tail (CT). In a comparison of monkey and chimpanzee tetherin sequences, the CT is less divergent than the TM and so this may be why the Nef protein was better able to adapt.

Since SIVcpz uses the Nef protein to counteract tetherin, it is surprising that HIV-1 uses Vpu. However, human tetherin has diverged from the chimpanzee protein, most notably owing to a deletion of a pentamer within the CT. As a consequence, the SIVcpz Nef protein is not active against human tetherin (Sauter *et al.* 2009). Clearly, this would have placed strong selection pressure on HIV-1, and this has resulted in the reacquisition of an anti-tetherin activity by Vpu. Perhaps the surprising aspect of this is that, while the Vpu protein of SIVcpz was not being constrained to retain anti-tetherin activity, nevertheless the *vpu* gene did not diverge to the extent that the activity could not be rescued.

Since the HIV-1 groups M, N and O each arose through separate transmissions of SIVs from apes, the selection pressure to counteract human tetherin would have been exerted on three independent occasions. This led to different outcomes. Only in the case of HIV-1 group M has adaptation been fully successful. In HIV-1 group O strains, neither Vpu nor Nef efficiently antagonize human tetherin (Sauter *et al.* 2009). HIV-1 group N Vpu has evolved to become active against tetherin, but this appears to have been at a cost. A second major function of Vpu is to bind to CD4 to induce its degradation. Unlike the anti-tetherin activity, this function seems to be highly conserved and not species-specific, perhaps because CD4 itself is less divergent among primates than is tetherin. However, HIV-1 group N Vpu has lost this anti-CD4 activity, possibly in the process of adaptation to an anti-tetherin activity. In summary, HIV-1 group M Vpu has two main functions: an anti-CD4 activity that was conserved from SIVcpz, and an anti-tetherin activity acquired since transmission to humans. HIV-1 group N has lost the first of these, while HIV-1 group O has not acquired the second. It is tempting to speculate that these differences may at least partly explain why group N and O viruses are quite rare, while group M viruses dominate the global AIDS pandemic (Sauter *et al.* 2009).

An alternative approach to seeking signatures of host-specific adaptation in HIV-1 is to look for similar genetic changes that occurred independently on each of the occasions when SIVs jumped into humans. Comparing the sequences of SIVcpz with those of the inferred ancestors of the three HIV-1 groups, we found one site in the proteome that was well conserved among SIVcpz but had changed, in the same way, on each of the three host jumps giving rise to groups M, N and O (Wain *et al.* 2007). Codon 30 of the *gag* gene encodes Met in all known strains of SIVcpz from central chimpanzees, and also in SIVgor. However, the inferred ancestral sequences of the three HIV-1 groups encode Arg at this position, implying that a radical amino acid replacement occurred on each of the three branches of the tree encompassing cross-species transmission to humans. Two lines of evidence provide corroboration that this site is involved in host-species-specific adaptation.

The first comes from an experiment in which a chimpanzee was infected with HIV-1; when the virus was sequenced 10 years later, this site had reverted to encoding Met (Mwaengo & Novembre 1998). Secondly, this chimpanzee-adapted HIV-1 virus was subjected to site-directed mutagenesis and then tested for replication in chimpanzee and human $CD4^+$ T-cells. Viruses differing only at codon 30 of *gag* grew with different efficiency in chimpanzee T-cells, with those encoding Met replicating faster; the opposite was observed in human T-cells (Wain *et al.* 2007). This part of the *gag* gene encodes the N-terminal domain of the matrix protein. The structure of this protein has been solved (Hill *et al.* 1996), and while there is considerable information about the interaction of the matrix protein with host proteins, there is as yet no clue as to the function of this particular residue or why chimpanzee and human hosts exert different selection pressures on it.

5. CONCLUSIONS

It has been possible to reconstruct a surprisingly detailed picture of the origins of pandemic AIDS (Sharp & Hahn 2008). The source of HIV-1 group M, the main form of AIDS virus infecting humans, has been traced to a virus infecting the central subspecies of chimpanzees, *P. t. troglodytes*, in a remote area in the southeast corner of Cameroon (Keele *et al.* 2006). The likeliest route of chimpanzee-to-human transmission would have been through exposure to infected blood and body fluids during the butchery of bushmeat (Hahn *et al.* 2000). The early diversification of group M appears to have occurred some 700 km further south, in Kinshasa (then called Leopoldville), in the early years of the twentieth century (Worobey *et al.* 2008). The links between these two regions are waterways, which were the major communication routes at that time: the rivers from southeast Cameroon flow south, ultimately joining the Congo River on which Kinshasa is located. Other viruses from central chimpanzees have been transmitted to humans, giving rise to HIV-1 groups N and O, and the prospective group P; among these, some (probably P, and perhaps O) may have been transmitted via gorillas. It is striking that all of these transmissions were derived from one subspecies of chimpanzee. Eastern chimpanzees also have SIVcpz, but descendants of those viruses have not been detected in humans, nor in gorillas that are sympatric with eastern chimpanzees (Takehisa *et al.* 2009). It is not clear that humans living in east central Africa are less likely to have been exposed to SIVcpz than those living in west central Africa. It is possible that the level of surveillance has been lower in east central Africa, and that rare strains of HIV-1 derived from the SIVcpz of eastern chimpanzees circulate undetected. Alternatively, given that it is clear that SIVcpz of central chimpanzees has had to adapt in various ways to spread in humans, it is possible that the divergent form of SIVcpz found in eastern chimpanzees has less potential to make these adaptations.

Considering HIV-1 and HIV-2 together, it appears that there have been at least a dozen independent transmissions of SIVs to humans. None of these appear older than HIV-1 group M: the common ancestor of HIV-1 group O has been dated to around the same time (Lemey *et al.* 2004), while those of HIV-2 groups A and B may have been a little more recent (Lemey *et al.* 2003). The opportunities for chimpanzee- or monkey-to-human host jumps have existed for hundreds or thousands of years, and it must be expected that many such transmissions occurred in the past. However, only in the twentieth century did such viruses spread to detectable levels in the human population. In west central Africa during the early part of that century, the destabilization of social structures by invading colonial powers (Chimis *et al.* 2000), the origin and rapid growth of major conurbations (Worobey *et al.* 2008) and the widespread use of injections (Pepin & Labbe 2008) may all have contributed to provide an unprecedented opportunity for dissemination of blood-borne viruses.

The finding that HIV-1 originated in our closest living relatives raises a number of issues. Gene sequences of humans and chimpanzees typically differ at less than 2 per cent of nucleotides. Despite this genetic similarity of humans and chimpanzees, it is apparent that SIVcpz was subject to pressures to adapt to its new human host. It is clearly of substantial interest to understand much more about the natural biology of SIVcpz infection and transmission in chimpanzees, and the extent to which the natural history of these viruses differs from HIV-1 in humans. It will be of particular interest to understand the extent to which co-infection with other viruses, bacteria, protozoa (such as *Plasmodium*) or multicellular eukaryotes (e.g. worms) influence the course of SIVcpz infection and pathogenesis. For example, there is some evidence that humans co-infected with HIV-1 and GBV-C (a seemingly non-pathogenic member of the Flaviviridae) remain asymptomatic longer than those infected by HIV-1 alone (Stapleton *et al.* 2004); close relatives of GBV-C have been found in chimpanzees (Adams *et al.* 1998; Birkenmeyer *et al.* 1998). Further comparisons of SIVcpz and HIV-1 infections may shed light on the viral and host factors responsible for disease progression and ultimately point the way to novel therapeutic interventions.

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1. After reading the article, briefly describe what do we really know about the origin of HIV?

2. Although HIV infects humans and causes AIDS, what evidence do the authors present that HIV originated in non-human primates?

3. What is the role of chimpanzees and its significance to answers questions regarding origin of HIV and AIDS in humans?

4. What arguments would you suggest against AIDS as a Zoonotic Disease

Prepare your individual responses by Day 6 and – small-group response due by end of day 8.

Self-Test 1: AIDS: Defining the Disease and Finding Its Cause

____ 1. Worldwide, what is the estimated total number of HIV infections through 2013?

a. 890 thousand
b. 50 million
c. 68 million
d. 81 million

____ 2. The estimated percent of new HIV infections now occurring in industrialized countries is:

a. 5%
b. 25%
c. 50%
d. 80%

____ 3. The estimated total number of deaths expected worldwide due to AIDS through the end of 2013:

a. 8 million
b. 30 million
c. 73 million
d. 94 million

____ 4. Select the most accurate statement.

a. HIV disproportionately affects vulnerable population groups
b. AIDS patients all have the same disease
c. The first U.S. AIDS cases occurred in gay men
d. The first reported AIDS cases in the U.S. were in men

____ 5. AIDS is often incorrectly referred to as a disease. It is, however, a syndrome. What is a syndrome?

a. A set of symptoms or diseases which occur together.
b. Appearance of microscopic organism when grown in media
c. Transmitability from infected host to uninfected host
d. Anything accompanied by a fever.

_____ 6. When AIDS was first reported, the most frequently occurring risk factor among gay men with AIDS was?

a. High frequency of engaging in anal sex.
b. Being a hemophiliac.
c. Use of drugs for sexual pleasure enhancement.
d. Many sex partners.

_____7.In 1983, French scientists discovered that the specific cause of AIDS was

a. Viral.
b. Sexually transmitted.
c. Transmitted through bodily fluids.
d. An opportunistic infection.

_____ 8. Which of the following cause immune system suppression?

a. HIV.
b. Radiation exposure.
c. Corticosteroids.
d. Alkylating agents.
All of the above

_____9. Of the 136 cases of HIV-2 that have been reported in the U.S., only about ___% have progressed to AIDS.

a. 20
b. 40
c. 60
d. 80

____ 10. Choose the <u>false</u> statement regarding the origins of HIV-2.

a. HIV-2 jumped into humans in the early 1940's.
b. HIV-2 is a direct genetic descendent of HIV-1.
c. HIV-2 came from Mangabey monkeys.
d. HIV-2 moved into humans near Canchungo City, Guinea-Bissau.

____ 12. One factor that distinguishes HIV-2 from HIV-1 is

a. it appears to be less harmful to T-cells.
b. it reproduces more rapidly.
c. its high viral load in the blood.
d. its origin in South Africa.

____ 13. When AIDS was first defined in 1982, upon which single characteristic was it based?

a. Kaposi's sarcoma
b. *Pneumocystis* pneumonia
c. Toxoplasmosis of the brain
d. There was no single characteristic.

____ 14. The CDC definition of AIDS has been changed several times. What was/were the objective(s) of such change?

a. Simplify classification of HIV infection.
b. Be consistent with standards of medical care for HIV infected people.
c. Better categorize HIV related morbidity.
d. More accurately reflect the number of people most in need of close medical attention due to severe HIV related immunosuppression.
e. All of the above.

_____15. Which of Koch's four postulates has not yet been fulfilled by HIV/AIDS research?

a. HIV must be found in all AIDS cases.
b. HIV must be isolated from the host.
c. HIV must produce AIDS when introduced into a susceptible host.
d. HIV must be found in the susceptible host it was introduced into.
e. All have been met.

_____16. Regarding the theory that HIV is a mutant of SIV, which statement is **false**?

a. SIV cannot infect humans.
b. SIV does not cause an AIDS-like illness in monkeys.
c. An SIV/HIV hybrid may have been in humans for thousands of years.
d. We don't know how SIV mutated into HIV.

_____17. The eleven distinct subtypes of HIV are designated by:

a. The year they were discovered.
b. The letters A-K.
c. The main symptom present.
d. The numbers 1-11.

____ 18. How many times is it believed that HIV-1 crossed from chimpanzees into humans?

a. 1
b. 3
c. 6
d. 11

____ 19. Select the **false** statement.

a. HIV-1, group M, subtype B is the most prevalent type of HIV in the U.S. and Europe.
b. The most prevalent type of HIV in Haiti arrived from Africa around 1966.
c. HIV spread from Haiti to the U.S. in one migration.
d. HIV arrived in the U.S. from Haiti for the first time by 1969.
e. None of the above.

____ 20. Which viruses have shown cross-species transfer?

a. Yellow fever
b. Dengue
c. Malaria
d. All of the above
e. HIV is the only cross-species transfer of a virus.

Introduction: An overview of AIDS

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What is AIDS

- Acquired Immune Disease Syndrome
- Recognized as a Syndrome in 32 Years ago (1981)
- AIDS refers only to the end stage of a progressive disease that starts with HIV infection and leads to severe impairment of the immune system

Clinical Definition of AIDS

- CDC defines AIDS in an adult or adolescent aged 13 years or older as the presence of **one of 25 conditions** that indicate that the immune system is severely compromised
- People with HIV are also defined as having AIDS once their CD4 + T cell count goes below 200 cells per cubic milliliter (pcm) of blood (normal CD4 counts are between 500 and 1600 pcm

Why AIDS is a Syndrome and not a Disease?

- The two terms are not applied rigorously AIDS is still called a "syndrome" even though we now have a good line on the cause, the HIV virus
- It acquired the name "syndrome" before the cause was known, and it has stuck.
- Others would say that the HIV infection is the disease, and that AIDS is the syndrome (set of symptoms) caused by it, because you can have the HIV infection without having AIDS
- The two terms overlap substantially and sometimes you can only tell what a particular

Syndrome vs Disease

Syndrome is a set of symptoms that all appear together

Disease is an illness where you have a line on the **cause** of it: genetic, toxicological, bacterial, viral, etc. Disease is impairment of health or a condition of abnormal functioning

Syndrome can indicate a disease, but not necessarily. It may be that you have several diseases, or several different diseases can all cause the same syndrome.

AIDS and Society

1. HIV and AIDS has devastated the whole region—increased medical costs and care for individuals
2. Reduced national development—because the economic resources have been directed towards infected individuals
3. Widened the gap between rich and poor—greater incidence of HIV infection and AIDS among poor people
4. Stigmatized groups have been marginalized in the society

HIV infection and AIDS: Endemic, Epidemic, and Pandemic

Endemic, Epidemic and Pandemic

The public health terms **endemic epidemic pandemic** all describe an illness by its prevalence and geographic location

Endemic: Present in a community at **all times** but in relatively **low frequency**. Something that is **endemic** is typically **restricted** or peculiar to a locality or region

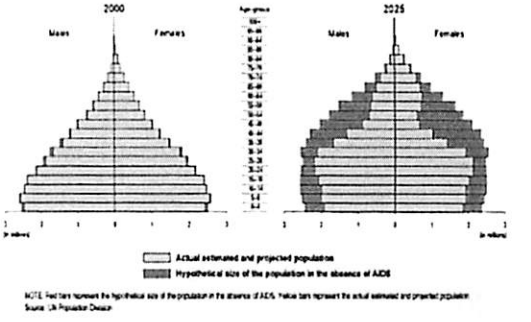
Epidemic: A sudden outbreak. The occurrence of more cases of a disease than would be expected in a community or region during a given time period. A sudden severe outbreak of a disease such as SARS. HIV is Epidemic. Whole region.

Estimated HIV prevalence in adults, by Global Region (2011)—Pandemic slow spread

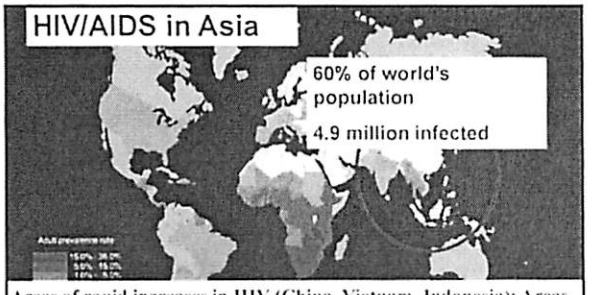
	HIV cases (estimate)	*Epidemic began*
N. America (4%)	1.4 million	1970s, 80s
Latin America, Caribbean (4.7%)	2.3 million	1970s, 80s
Africa (69%)	23.5 million	1970s,80s
Asia (12%)	4.0 million	late 1980s
Western Central Europe (3%)	0.9 million	1970-80s
Eastern Europe (4%)	1.4 million	1990s
Middle East 1%	0.3 million	1990s
East Asia/Oceania (2.2%)	0.89 million	1990s

Global Total **34.6 million living with HIV and 30 million have died due to AIDS related causes**

Population size with and without AIDS, South Africa, 2000 and 2025



HIV/AIDS in Asia



Areas of rapid increases in HIV (China, Vietnam, Indonesia); Areas of sustained epidemic levels (India, Myanmar); areas of HIV declines (Thailand, Cambodia), and low prevalence countries (Laos, Pakistan, Sri Lanka, Philippines).

Overview: Biological Agents

What is a Pathogen? = Disease Causing Agent

- Viroid—Naked Nucleic acids (agent)
- Virus—A-cellular Nucleic acid + Protein (agent)
- Prions—Only Proteins (agent)
- Mycoplasma—Small Bacteria with no Cell wall
- Bacteria—Unicellular (organism)
- Protozoa—amoeboid structures (organism)
- Fungi—Non-photosynthetic (organism)