Jacques Leibowitch in Wikiipédia (version en anglais)

'''Jacques Leibowitch''' ((born August 1st 1942) is a medical doctor and clinical researcher known for his contributions to the knowledge and treatment of [[HIV]] and [[AIDS]], starting with his initial designation of a human [[retrovirus]] as the cause of AIDS, and his ground-breaking use of of [[triple combination therapy]] for the effective control of HIV in the patient. A practicing physician in the infectiology department of the [[Raymond-Poincaré hospital]] of [[Garches]] (directed by Prof. Christian Perronne, AP-HP), University lecturer Emeritus, he currently leads the treatment program ICCARRE that proposes a dramatic reduction of weekly anti-HIV drug intake, down to 2-3 anti-viral pills a day taken 2 to 3 or 4 days a week, as opposed to the presently recommended seven days a week, as still universally prescribed. These reduced medical dosages are adequate, necessary and sufficient according to the results of his exploratory clinical research carried out since 2003.
He is the author of the books "Un virus étrange venu d'ailleurs" ("A strange virus of unknown origin")<ref>[http://www.plon.fr/ouvrage/pour-en-finir-avec-le-sida/9782259207591 "Pour en finir avec le sida", Jacques Leibowitch, 2011, sur le site de l'édition Plon. Consulté le 1/10/2013]</ref>, and "Pour en finir avec le sida" ("Putting an end to AIDS")<ref>[http://www.decitre.fr/livres/un-virus-etrange-venu-d-ailleurs-9782246333319.html "Un virus étrange venu d'ailleurs", Grasset 1984]</ref>.

==Biography==
Jacques Leibowitch did his medical studies in Paris (1960-1968), and did his physician training at the AP-HP hospitals (1969-1979) where he majored in clinical immunology, notably at the Necker hospital under Professor Jean Hamburger.
He acquired his initial experience in research in 1962 at the Bellevue Hospital of New York, later returning to the United States for a Post-doctoral research program at Harvard Medical School (Pr John David, Robert Brigham Hospital, Boston, 1970-1972), where he studied cellular immunology<ref>[http://www.histrecmed.fr/index.php?option=com_content&view=article&id=64:leibowitch-jacques&catid=8:entretiens&Itemid=101 Entretien avec Jacques Leibowitch réalisé par J.-F. Picard en mai 2001 sur le site histrecmed]</ref>. On his return to Paris, he finished his internship and went on to research Human Complement Biology at the Royal Hammersmith Hospital, London as post-graduate medical registrar (Pr Keith Peters, 1973-74), before undertaking his senior residency in nephrology at Necker, entering the Raymond Poincaré hospital at Garches as immunology assistant lecturer (1980).
Jacques Leibowitch has published many [http://www.ncbi.nlm.nih.gov/pubmed/?term=leibowitch+j articles in

international scientific journals] that can be consulted on Pubmed.

==Scientific and medical contributions==

The contributions of Jacques Leibowitch have marked the history of HIV and AIDS and their treatment<ref>[http://www.valas.fr/Jacques-Leibowitch-Pour-en-finir-avec-le-SIDA,230 Les contributions de Jacques Leibowitch "Pour en finir avec le sida", sur le site de Patrick Vallas. Consulté le 1/10/2013]</ref>:
* In 1982, he expounded the hypothesis that an exotic CD4 trope retro-virus might be at the origin of the growing AIDS epidemic and put the Montagnier and de Gallo teams on the track of the virus
* In 1984-1985, he removed from the Cochin hospital blood transfusion center the HIV contaminated blood samples, using a test quickly developed under the urgency of the situation by Dr Dominique Mathez, Leibowitch's main collaborator at the Raymond Poincaré hospital at Garches, anticipating the large-scale screening tests.
* Leibowitch and Dr. Mathez developed a home-made biological assay system to measure precisely the levels of active virus in the patient before and under treatment, demonstrating the both meager and transient effectiveness of the antiviral AZT as monotherapy.
* He is the father in Europe of the first anti-HIV treatments combining three anti-viral molecules (tri-therapy treatment) for the long-term control of HIV in the correctly treated patient.
* From 2003 to 2014, he has shown that after a minimum six-month period on conventional 7 day-a-week "attack" treatment, weekly anti-viral drug intake could be reduced by 40 to 80%, while maintaining optimal control over the patient's HIV.

===Discovery of the HIV retro-virus===

Jacques Leibowitch is at the center of the research on AIDS since the original outbreak of the epidemic, from the very moment when the investigation on its causative agent was launched. When the first series of AIDS cases in the United States were published in the New England Journal of Medicine and the Lancet in December 1981, Leibowitch noticed the similarity between the cases described in the United States and the historic case of a multiple-opportunistic infection syndrome in a Portuguese resident in Paris who had spent time in Angola and Mozambique between 1973 -76. He was then contacted by Willy Rozenbaum in March 1982 to set up the informal French Working Group SIDA, a self-nominated body to analyse the cases appearing in France.
When in July 1982, the first cases of AIDS appear in hemophiliacs receiving highly filtered blood samples, the scientific community realized that ~~the causal agent of~~ AIDS was most likely caused by a virus. Jacques Leibowitch noticed some intriguing similarities between AIDS and the pathology linked to HTLV

(Human T Cell Leukemia Lymphoma Virus), the only known human retro-virus at that time. Both situations affect CD4 T helper lymphocyte cells. HTLV induces the massive proliferation of one or several clones and their cancerization, whereas the other virus, the HIV virus ~~appears~~ tends to eradicate these cells without apparent discrimination <ref>Un entretien avec le Docteur J. Leibowitch, "Le Panorama du médecin" n°1507, 8 octobre 1982</ref>. Otherwise, these two pathological descriptions are present in both Africa and the Caribbean (see. A Strange Virus of Unknown Origin Jacques Leibowitch, Ballantine Books, New York, 1985, translated from Un Virus Etrange Venu d'Ailleurs, Grasset Paris 1984). Indeed, in both Paris and Brussels, doctors had seen cases of patients having lived or spent time in Francophone Africa or in Haiti who suffered from a disease with an undeniable resemblance to that arising at the time in the United States in "immuno-deficient homosexuals". Leibowitch, informed by the Franco-American literary author Gilles Barbedette of the announcement by Robert Gallo in Medical World News (August 1st 1982) that an HTLV type retro-virus could be at the cause of AIDS, found in that most succinct brief the profile matching his CD4-tropic exotic viral suspect (in Grasset, Ballantine Books, workS cited). The retro-viral inspiration was thus consolidated and opened between Bethesda (Gallo) and Paris (Leibowitch et al.) from August 1982 onwards.
Failing to find in the Paris team of Professeur Jean-Paul Lévy <ref>[http://www.histrecmed.fr/index.php?option=com_content&view=article&id=65:levy-jean-paul&catid=8:entretiens Entretien avec Jean-Paul Lévy réalisé par Anne Lévy-Viet&Jean-François Picard, janvier 1992-décembre 2001, paragraphe "Mais vous-même, vous aviez reçu la visite des cliniciens à Cochin" sur le site histrecmed]</ref> or the Lille team of Dominique Stéhelin a French retro-virus specialist eager to pursue this line of investigation, he contacted upon a recommendation by Jean Paul Lévy Professor [[Robert Gallo]]<ref>[http://history.nih.gov/NIHInOwnWords/docs/gallo2_02.html Interview with Robert Gallo réalisé par Victoria A. Harden et Dennis Rodrigues le 4 novembre 1994 sur le site de l'Office of NIH History]</ref> in Bethesda, the then world renowned virologist on HTLV. It was then in November 1982 that Gallo informed him from Bethesda of his initial virology findings in keeping with the AIDS HTLV-type virus hypotheses. For his part, Willy Rozenbaum, warned in private by Leibowitch that an exotic ~~que~~ HTLV-type retrovirus could well be the cause of AIDS, embarks upon a discreet collaboration with the Luc Montagnier team of the Pasteur Institute. Montagnier, along with his collaborator Jean-Claude Chermann, had just recently received news of the HTLV and AIDS hypotheses by Dr Paul Prunet, the then director of « Recherche&Développement » at Sanofi-Pasteur-Marnes La Coquette, where Leibowitch had given a speech at the end of November 1982 <ref>[http://www.valas.fr/IMG/pdf/6-Prunet_Paul_2.pdf Paul Prunet,"Comprendre la vie et ou comprendre les maladies. Avec petit retour sur l'histoire de la recherche sur le sida en France" sur le site de Patrick

Valas]</ref>. The Montagnier team subsequently detected in the cell culture of patient BRU the traces of the first non HTLV retrovirus in January 1983, a virus eventually recognized as the cause of AIDS thanks to the conclusive additions by Robert Gallo and his group (April 1984) [http://quod.lib.umich.edu/c/cohenaids/5571095.0541.047/1?page=root;rgn=full+text;size=100;view=image"Memo Regarding Chronological Summary of Experiments Leading to the Isolation of HTLV-III from AIDS and ARC" sur le site de la Jon Cohen AIDS Research Collection, 2 pages]</ref>. [[Luc Montagnier]] and Françoise Barré-Sinoussi received the Nobel Prize for Medicine in 2008 for their work. In a letter to the prestigious magazine Nature Medicine in 2003, as well as in his Nobel Prize acceptance speech in 2008, Luc Montagnier recognizes Jacques Leibowitch as being the initiator of the retro-virus hypothesis in France <ref>[http://www.nature.com/nm/journal/v9/n10/full/nm1003-1235a.html Luc Montagnier, 2003, "Historical accuracy of HIV isolation", Nature Medicine 9]</ref>{{,}}<ref>[http://www.nobelprize.org/nobel_prizes/medicine/laureates/2008/montagnier_lecture.pdf Luc Montagnier, "Nobel lecture", 2008]</ref>. However, the patented list of the discoverers of AIDS and HIV do not take Jacques Leibowitch into account for his contribution in the initial phases of the discovery. The scientific historian [[Mirko Grmek]] reflects back on the details of the stages that led to the discovery of the AIDS virus in his work “the History of AIDS” and the [http://www.joncohen.org/Jon_Cohen/archive.html Jon Cohen AIDS Research Collection] contains numerous archived documents on the subject. The book “Sida.O” (AIDS.O) written by D. Lestrade and G.Pialoux contains also many details on the history of AIDS <ref>[http://www.fleuvenoir.fr/site/sida_20_&100&9782265094529.html Didier Lestrade et Gilles Pialoux, "Sida 2.0, Regards croisés sur 30 ans d'une pandémie"]</ref>.

===Detection and elimination of HIV-positive contaminated blood at Garches and at Cochin===

In 1984, whilst Luc Montagnier is working at the Institut Pasteur on an industrial test for HIV antibodies, Dominique Mathez and Jacques Leibowitch are working at Garches to elaborate a working test on tumour cells infected by the HTLV-III given to them by Pr Daniel Zagury at Paris University on behalf of Robert Gallo. Using this craftsman test, Mathez and Leibowitch discover a disturbing frequency of individuals contaminated by the retro-virus amongst the polytranfusion recipients, and later, in collaboration with Dr François Pinon, head of transfusions at the Cochin hospital, go on to discover, the alarming proportion of HV positive blood donors (1 in 200) in a pilot study carried out on {{formatnum:10000}} donors in the Paris and Ile-de-France area. The health authorities were alerted on this issue together with their dramatic

consequences for hemophiliacs (« if the Cochin Hospital study is correct, then all anti-hemophiliac stocks are contaminated … », Jean Baptiste Brunet at the French General Directory on Health, Mars 1985
13<ref>[http://www.larecherche.fr/actualite/aussi/retour-affaire-du-sang-contamine-01-06-1996-77500 "Retour sur l'affaire du sang contaminé" par Catherine Manuel et Pascal Auquier, 1/06/1996, site de "La recherche"]</ref>). It was thanks to this artisanal test that 50 HIV positive blood donations, established then to be 100% contaminating, were taken out of the transfusion process, and 150 potential receivers of this blood were protected from contamination <ref>[http://www.liberation.fr/societe/1999/02/17/le-proces-du-sang-contamine-5e-jour-des-lenteurs-organisees-par-nos-ministres-contaminee-par-transfu_265222 "Le procès du sang contaminé. 5e jour" par Eric Favereau et Armelle Thoraval, "Libération" le 17/02/1999]</ref>.

===Measure of viral levels in patients and evaluation of the effectiveness of treatment===
At Garches, Dominique Mathez and Jacques Leibowitch develop a sophisticated and reliable biological test enabling them to quantify active HIV virus levels in patients both before and during their antiviral treatment. Indeed, from 1987, patients in France most affected by the virus receive AZT treatment in the hope that this molecule might block the reproduction of the virus. It was with the aim of monitoring the progressive decline of virus levels in the treated patient that the team at Garches works on their method. Leibowitch presents to world specialists assembled for the conference at Marnes la Coquette (Pasteur-les Cent Gardes symposium, November 1989) his results showing that the AZT monotherapy becomes quickly ineffective as demonstrated by returning viral levels in the treated patient, though in the first month such levels were significantly, yet only transiently, reduced. The measuring of HIV viral levels is later to become, in its commercial and industrial version, the universally used test to follow the development of the virus and the effectiveness of various treatments. Also, Jacques Leibowitch is the first in France to collect sequential cell specimens from individual patients at follow up, preserving living cell samples at extremely low temperatures since 1982. This live-frozen cell bank would later become a precious for retrospective scientific investigations.

===First tri-therapy trials based on viral end-point levels, “Stalingrad trials, the besieged retrovirus” (Libération, August 2013)===
Jacques Leibowitch is the father of the tri-therapy treatments in Europe <ref>[http://www.liberation.fr/culture/2013/08/02/essai-stalingrad-le-virus-assiege_922481 "Essai "Stalingrad", le virus assiégé" par Eric Favereau, "Libération" du 3 et 4 août 2013]</ref>. Following the failure of AZT monotherapy to control HIV in the patient, the dual antiviral therapy (bi-therapy) soon reveals itself in Mathez and Leibowitch’s pioneering test to be

hardly more effective, thanks to the evidence revealed by the viral charge test at Garches. It is at this moment in 1994 that a new family of anti-HIV drugs emerges: the anti-proteases.
Having observed in vitro the spectacular results of three combined anti-HIV nucleoside analogues (AZT +3TC +DDI) available for clinical use at the time (July 1994) and seen in patients the most effective antiviral impact of a first ever triple combination of nucleoside analogues (as shown by his home-made viral load quantitation system), Jacques Leibowitch went on to test the efficacy of ~~a new family of anti-HIV drugs -~~ the anti-proteases … combined with pairs of nucleoside analogues to form a mixed-type triple combination therapy. On that basis, Leibowitch launches the Stalingrad Trial based on AZT+DDC+Ritonavir, a trial carried out in collaboration with Abbott, industrial producer of the anti-protease Ritonavir, under the protection of Health Minister Philippe Douste Blazy, outside the influence of the Agence Nationale de Recherches contre le SIDA (ANRS)
<ref>[http://editions.ehess.fr/ouvrages/ouvrage/sida-la-course-aux-molecules/ "Sida : la course aux molécules". Sébastien Dalgalarrondo,2004; Editions EHESS]</ref>. The results of the Stalingrad trial underlined the major importance measuring viral levels in real time in the patient in order to evaluate the impact of a given antiviral treatment. The success of this first tri-therapy treatment in the world is presented, together with that of another tri-therapy carried out by the group Merck, at the Washington Congress in February 1996. The findings are published in a scientific journal in 1997<ref>[http://www.ncbi.nlm.nih.gov/pubmed/11322272 Reductions in viral load and increases in T lymphocyte numbers in treatment-naive patients with advanced HIV-1 infection treated with ritonavir, zidovudine and zalcitabine triple therapy, "Antivir Ther." 1997 Jul;2(3):175-83]</ref>.

The tri-therapy treatment has since been heralded a major turning point in the history of treatment of HIV infection.

===Working towards an adjustment of maintenance treatments to adequate and sufficient dosages with the ICCARRE program===
Since 2003, Jacques Leibowitch has been carrying out a pilot study aiming to diminish anti-HIV doses within weekly cycles. With ICCARRE
<ref>[http://www.iccarre.org/ En savoir plus sur le protocole ICCARRE sur le site dédié]</ref>(French abbreviation: Intermittent, in Short Cycles, the Anti Retrovirals may Retain Effectiveness), just under one hundred HIV positive patients at the Raymond Poincaré hospital have undergone reduced treatment maintenance therapy reduced 4, or 3, or 2, or even 1 day a week, instead of the currently universally obligatory dosages of 7 out of 7 days, without the virus reappearing. ICCARRE has yet to be validated by regulatory bodies as a recommended anti-HIV regime; were its dosages and recommendations to be confirmed in future prospective clinical trials, the ICCARRE study would open

a new avenue in anti-HIV long-term therapy.

According to the ICCARRE regime: following an early initial period in which control of retro-viral levels requires 7-day-a-week “attack treatment” during one semester or more, weekly anti-viral dosages, necessary and sufficient to achieve effective long term control of the virus, may be administered in weekly reduced dosage; such a regime offers a number of advantages including : adhesion to the deontological principal of not exceeding required medicine dosages ; minimization of the toxic effects of these heavy chemical treatments over a long-term period ; improved willing patient acceptance of an effective treatment due to a physiologically and psychologically more acceptable programme ; reduction from between 40 and 80% of treatments that become exorbitantly costly over the long term. The first results of the ICCARRE study on 48 patients from Garches were published in 2010<ref>[http://www.fasebj.org/content/24/6/1649.long#ref-7 Short cycles of antiretroviral drugs provide intermittent yet effective therapy: a pilot study in 48 patients with chronic HIV infection, "FASEB J.", 2010, Leibowitch "et al".]</ref> ; as were those of three other withdrawal trials of this kind with shorts cycles carried out successfully by [[Anthony Fauci]] "et al." <ref>[http://www.pnas.org/content/98/26/15161.abstract Short-cycle structured intermittent treatment of chronic HIV infection with highly active antiretroviral therapy:effects on virologic, immunologic, and toxicity parameters, "PNAS", 2001, Dybul "et al".]</ref>{{,}}<ref>[http://www.jstor.org/stable/30076801 A proof-of-concept study of short-cycle intermittent antiretroviral therapy with a once-daily regimen of didanosine, lamivudine, and efavirenz for the treatment of chronic HIV infection, "JID", 2004, Dybul "et al".]</ref>{{,}}<ref>[http://www.plosone.org/article/info:doi/10.1371/journal.pone.0010307 A randomized, controlled, trial of short cycle intermittent compared to continuous antiretroviral therapy for the treatment of HIV infection in Uganda, "Plos One", 2010, Reynolds "et al".]</ref>, at NIH NIAID in the United States.

In his interview of 1st December 2011, on BFM Business, and his appearances on the television show of Michel Drucker ("Vivement dimanche" May 24th 2013 <ref>[http://www.france2.fr/emissions/vivement-dimanche/diffusions/19-05-2013_58693 Emission "Vivement dimanche du 24 mai 2013" sur le site de France2]</ref>) and Laurent Ruquier ("On n'est pas couchés " June 15th 2013 <ref>[http://lemediascope.fr/video-france-2-ruquier-le-pr-jacques-leibowitch-on-nest-pas-couches-15-juin-2013/ Video "France 2-Ruquier/le Pr Jacques Leibowitch" "On n'est pas couchés"(15 juin 2013), sur le site Le mediascope, consulté le 1/10/2013]</ref>), Jacques Leibowitch has presented his programme of « canny short cycles », which distinguish themselves from current recommendations, which advocate the intake of medications on 7 days out of 7<ref>[http://www.podcasters.fr/episodes/bfm-business-professeur-jacques-leibowitch-16524674.html BFM Business :

Professeur Jacques Leibowitch]</ref>{{,}}<ref>{{Lien web |auteur= |titre=Leibowitch chez Drucker. Retranscription sur le site sero-on-line |url=http://www.sero-on-line.org/forum/viewtopic.php?t=11151 |consulté le=7 août 2013}}</ref>.

==Distinctions==
*Chevalier of the Legion of Honor, 1993

==Publications==
*Un virus étrange venu d'ailleurs Jacques Leibowitch, Grasset, 1984 ; translated for Ballentine Books, New-York, 1985 as : A Strange Virus Of Unknown Origin),

*Pour En Finir Avec Le SIDA (Putting an end to AIDS), Jacques Leibowitch, Plon, 2011

== References ==
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