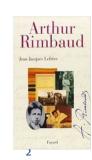
# In the memory of Jean Jacques Lefrère Passive immunotherapy for AIDS

Farhad Heshmati
MD, PhD
WAA/SFH joint congress
Paris, April 27-29 2016

Doctor Jean Jacques Lefrère Hematologist, Researcher

And

Mister Lefrère Writer

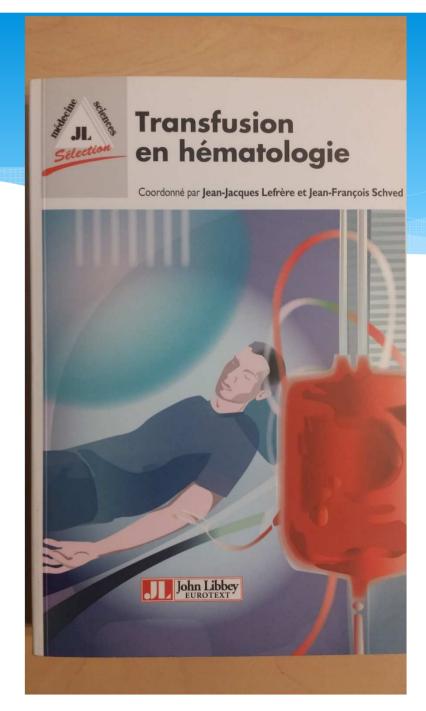




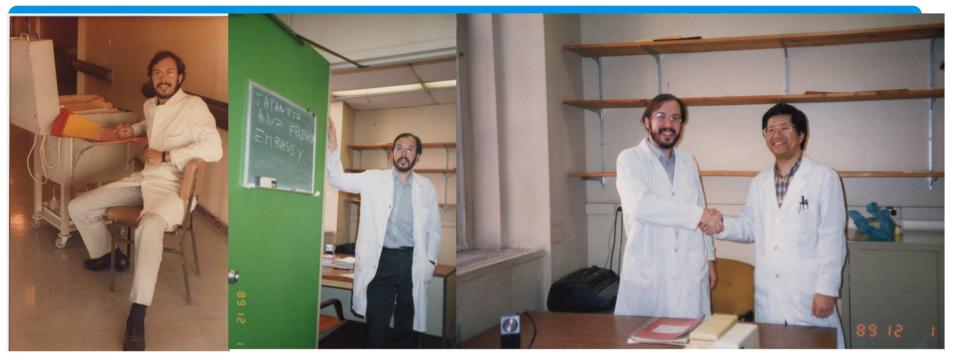
### Jean Jacques Lefrère

- Professor of Hematology at the Paris Descartes
  University
- \* Director of the National Institute of Blood Transfusion
- \* National expert in transfusion and transfusion security, prions, viruses, transmissible agents by blood transfusion,
- \* More than 300 papers in international reviews
- \* Many medical books
  - \* use of the blood components
  - \* transfusion in Hematology





F Heshmati. in the memory of JJ Lefrère. WAA/SFH 2016







# He was a pioneer of Passive Immunotherapy in AIDS

# Plasma therapy against infectious pathogens, as of yesterday, today and tomorrow

O. Garraud, F. Heshmati, B. Pozzetto, F. Lefrere, R. Girot, A. Saillol, S. Laperche

Transfusion Clinique et Biologique, Vol 23, N° 1, 39-44, Fev 2016

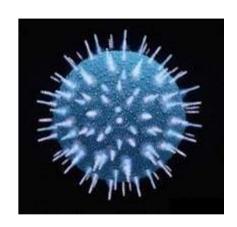


- \* Plasma therapy consists in the transfusion of plasma to patients generally suffering from a severe infection, in the absence of curative treatment.
- \* Plasma is obtained from:
  - \* either voluntary healthy immunized individuals
  - \* or convalescent persons
- \* Plasma therapy has been used since the Spanish flu in 1917–1918, and then regularly when viral epidemics threatened vulnerable populations, the last reported occurrence being the 2013–2015 Ebola virus outbreak in West Africa.

#### HIV Global Pandemia

In the 1980<sup>th</sup> decade, a terrible and lethal viral epidemic appeared: AIDS epidemic

- We learned soon that:
- \* It is due to a virus (1984)
- \* The serological screening is possible (1985)
- \* The progression is slow
- Terminal issue is always lethal
- \* There is no efficient vaccine (until now)
- \* No efficient treatment
- First anti-retroviral drug, Zidovudine (1987)
- \* In 1999 (WHO): AIDS was the 4<sup>th</sup> main cause of death worldwide and number one killer in Africa. 14 millions people had died from AIDS since the start of the epidemic.



# Courageous idea for passive Immunotherapy for AIDS

- \* The only available drug was Zidovudine (1987)
  - \* Its efficiency was limited by time
  - \* Responsible of the emergence of resistant viruses
  - \* Issue was lethal
- \* Decrease and vanishing of anti P24 Ab was accompanied by the progression of the disease (Alesi -1989).
- \* The idea for using the plasma Ab for terminal-phase patients by J.J. Lefrère and D. Vittecoq was proposed

Proc. Natl. Acad. Sci. USA Vol. 92, pp. 1195-1199, February 1995

Passive immunotherapy in AIDS: A double-blind randomized study based on transfusions of plasma rich in anti-human Immunodeficiency virus 1 antibodies vs transfusions of seronegative plasma

D. Vittecoq,

F. Heshmati J.J. Lefrère

### IP002 from 1990

- \* Randomized double-blind controlled trial
- 86 symptomatic patients randomized to receive plasma rich in anti-HIV1 Ab or standard seronegative plasma
- \* 300 ml plasma perfusion every 14 days for 1 year and then every 28 days
- \* Zidovudine and other conventional prophylactic treatments were associated

#### Donor selection

- \* Plasma donors were selected among symptomless seropositive individuals with > 400x10<sup>6</sup> CD4 lymphocytes
- \* Negative P24 Ag
- \* High anti-P24 concentration
- \* Negative for other standard serological screening
- \* Plasma were heat-inactivated before infusion (56° C, 30 min)

#### Results 1

Clinical benefit from passive immunotherapy was observed in:

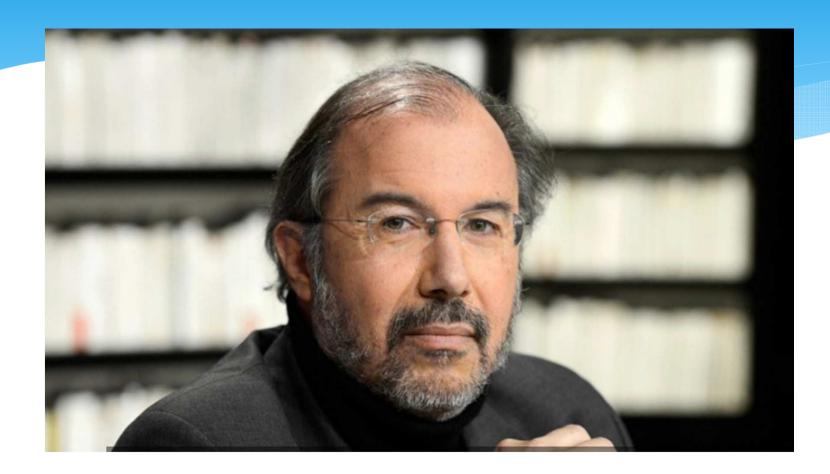
- \* Delaying the appearance of first AIDS-defining events (p<0,009)
- \* Reducing cumulative incidence of such events (3 fold)
- \* 7 deaths in the treatment group vs. 11 in the control group (p = 0,27)
- \* Less hospitalization

#### Results 2

- \* 47 patients died or exhibited new AIDS-defining event, 18 in the treatment group and 29 in the control group (p = 0,009)
- \* No clinical benefit after 1 year period
- \* No side effects in plasma donors

Doctor Lefrère
during the days of the week
and
Mister Lefrère
literature writer during WE

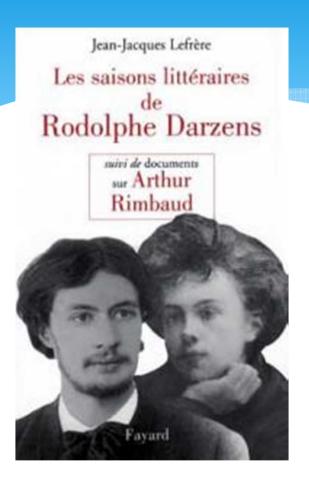




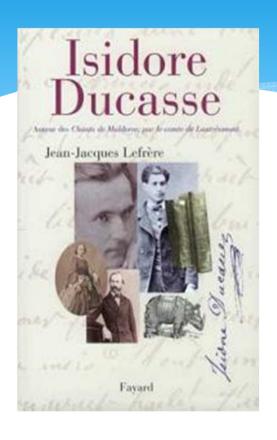


## Jean Jacques Lefrèrer Rimbaud's Doctor

- \* Biography and 1300 pages of documents on the Poet Rimbaud
- \* Anthology of Pia and Caradec
- \* Books on Lautréamont and Laforgue



Les Saisons littéraires de Rodolphe Darzens suivi de Documents sur Arthur Rimbaud
Jean-Jacques Lefrère
Sciences humaines
Parution:
27/05/1998

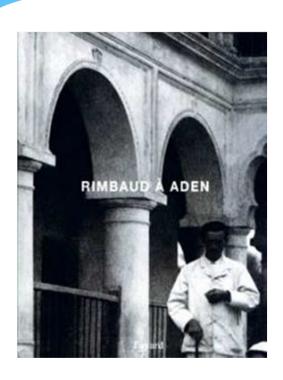


Isidore Ducasse
Jean-Jacques Lefrère

Histoire

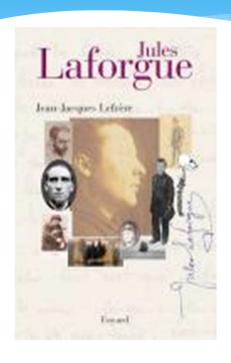
Parution:

27/05/1998



Rimbaud à Aden
Jean-Jacques Lefrère
Jean-Hugues Berrou
Pierre Leroy

Histoire Parution: 03/05/2001



Jules Laforgue Jean-Jacques Lefrère

2005



Rimbaud au Harar Jean-Jacques Lefrère

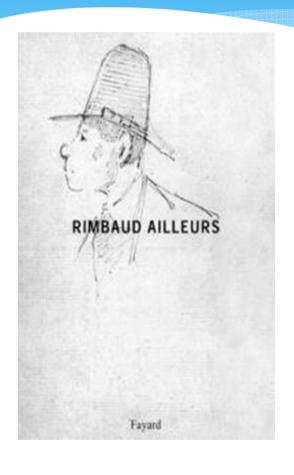
Histoire

Parution:

24/04/2002



Che Guevara, images
Jean-Jacques Lefrère
Jean-Hugues Berrou
Témoignages/Doc/Actu
Parution:
01/10/2003



Rimbaud ailleurs

Jean-Jacques Lefrère

Jean-Hugues Berrou

Pierre Leroy

Histoire Parution: 26/05/2004

Jean-Paul Goujon Jean-Jacques Lefrère

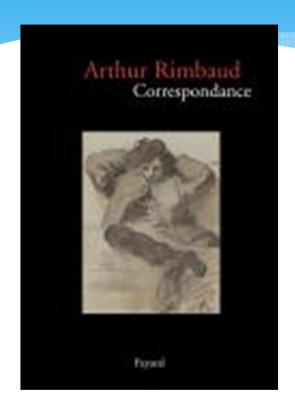




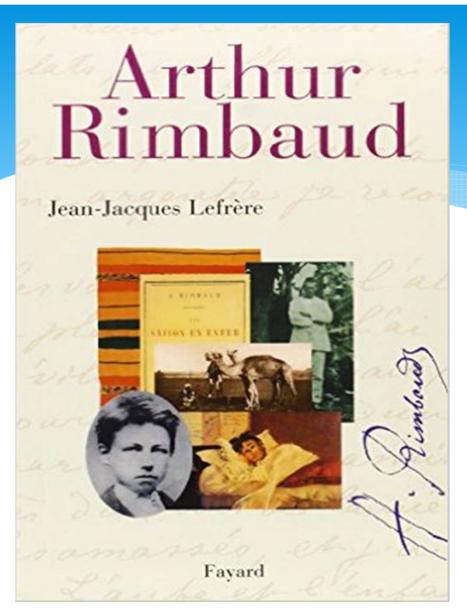
L'énigme Corneille-Molière

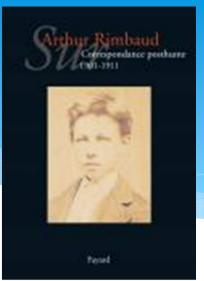
Fayard

Jean-Jacques Lefrère
Jean-Paul Goujon
'Ôte-moi d'un doute...
2006



#### Arthur Rimbaud Correspondance 2007

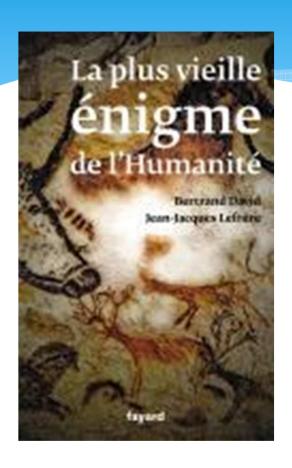




Arthur Rimbaud Vol 1: 2010



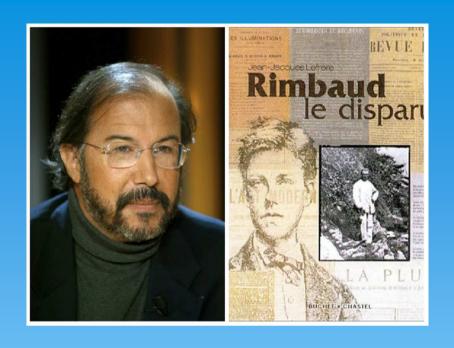
Arthur Rimbaud Vol 2: 2011



# La plus vieille énigme de l'humanité

Jean-Jacques Lefrère

2013



## April 16, 2015

As told Rimbaud: «... l'horloge de la vie s'est arrêtée tout à l'heure. Je ne suis plus au monde...»,

The life clock stopped just now, I'm not here any more

