

Health care-associated viral infections transmitted by blood

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Conditions required for a virus to represent a blood-born risk

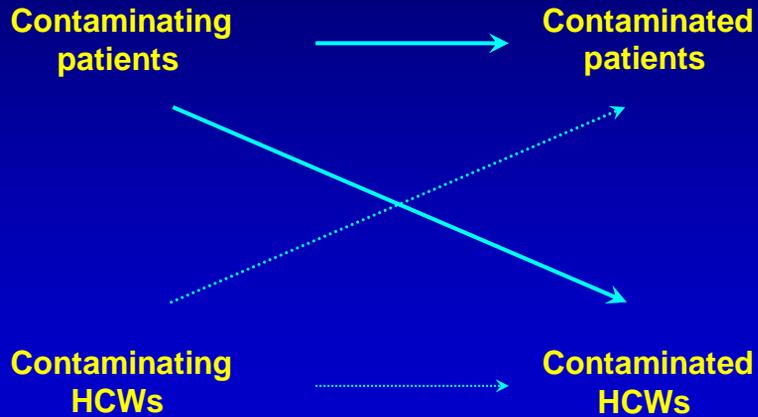
- to be able to establish a prolonged viraemia
- to exhibit a demonstrated risk of transmission
- to generate an identified and severe pathology, which excludes the following agents:
 - torquetenovirus (TTV)
 - GBVc/HGV

Plan of the presentation

- **A model of blood-borne virus: the hepatitis C virus (HCV)**
- **Four topics in relation with actuality:**
 - **transmission of blood viruses from HCWs to patients**
 - **transmission of arboviruses in relation with labile blood products**
 - **transmission of viruses via organ and tissue grafts**
 - **nosocomial dissemination of agents of viral hemorrhagic fevers**

A model of blood-borne virus: the hepatitis C virus (HCV)

Direct at-risk situations



Different kinds of HCV nosocomial risks

- Direct patient-to-HCW transmission
 - percutaneous route
 - mucosal route (exceptional)
- Indirect patient-to-patient transmission
 - injection of blood products
 - organ and tissue transplantation
 - haemodialysis
 - endoscopy...
- Direct HCW-to-patient transmission



Direct patient-to-HCW transmission: epidemiology



- Overall prevalence of HCV infection only slightly increased compared with the general population
- Factors associated with increased risk:
 - increasing age
 - increasing number of years in a health care occupation
 - history of transfusion of blood products
 - having sustained needle stick injuries
- Route of transmission:
 - mainly parenteral exposure (typically injury with a hollow-bore, injection-style needle contaminated with blood from an infected patient)
 - anecdotal routes of contamination:
 - mucosal splashes (2 cases)
 - punch (1 case)
 - human bite (2 cases)

Direct patient-to-HCW transmission: epidemiology



- Results of longitudinal studies (Henderson, Clin Microbiol Rev, 2003, 16, 546)

Reference	Yr	Location	No. of parenteral HCV exposures	No. of HCV infections	% Of subjects infected	Testing method(s) ^a	Comments
Kiyosawa ^b (174)	1991	Japan	110	3	2.7	EIA-1, RIBA-1	
Francavilla (116)	1992	Italy	30	0	0	EIA-2	
Hernandez (152)	1992	Spain	81	0	0	EIA-2, RIBA	
Marracconi (210)	1992	Italy	117	3	2.6	EIA, RIBA	
Mitsui (223)	1992	Japan	68	7	10.0	EIA-2, PCR	
Stellini (320)	1993	Italy	30	0	0	EIA-1, RIBA-1, PCR	
Sodeyama (318)	1993	Japan	62	3	4.8	EIA-2	
Sodeyama (318)	1994	U.S.	50	3	4.2	EIA-2, SN	
Lanphear (187)	1994	U.S.	53	1	2.0	EIA-2, EIA-3	
Perez-Trallero (244)	1994	Spain	61	0	0	EIA-2, RIBA-2	Dialysis settings
Petrosillo (249)	1994	Italy	123	2	1.6	EIA-2, RIBA-2	HIV-coinfected sources
Ippolito et al. ^c	1994	Italy	24	0	0	EIA-2, RIBA-2	
Zuckerman (380)	1994	U.K.	24	0	0	EIA-2, RIBA-2	
Puro (268) ^d	1995	Italy	97	1	1.0	EIA-2, RIBA-2	
Puro (269) ^d	1995	Italy	436	4	0.6	EIA-2, RIBA-2	
Puro (270) ^d	1995	Italy	61	0	0	EIA-2, RIBA-2	HIV-uninfected sources
Arai (18)	1996	Japan	56	3	5.4	RIA-1, PHA-2, PCR	
Mizuno (223)	1997	Japan	37	2	5.4	EIA-2, PCR, sequencing	
Serra (309)	1998	Spain	443	3	0.7	EIA-2, EIA-3	
Takagi (309)	1998	Japan	251	4	1.6	EIA-1, EIA-2, PCR	
Veeder et al. ^e	1998	U.S.	9	2	22.2	EIA, PCR	
Hamid (137)	1999	Pakistan	53	2	3.8	EIA-2, PCR	
Husan (140)	1999	Kuwait	24	0	0	EIA-2, RIBA	
Baldo (22)	2002	Italy	68	0	0	EIA-3, RIBA-2, PCR	
Regez (277)	2002	Netherlands	23	0	0	EIA-3, RIBA-2	
Wang (277)	2002	Taiwan	13	1	7.1	EIA-3, RIBA-2	
TOTAL			2,357	44	1.9		

Direct patient-to-HCW transmission: recommendations



- **Primary prevention**
 - respect of standard precautions (+++)
 - exposure avoidance (including injection devices intended to reduce occupational risk)
- **Post-exposure strategy**
 - immediate cleaning and decontamination of the exposure site
 - adequate reporting to the Occupational Medicine and correct follow-up of HCV antibodies and alanine aminotransferase levels (control at the time of exposure and at 3, 6 and even 12 months post-exposure)
 - identifying and testing the source patient for blood-borne pathogens (with his/her consent)

Indirect patient-to-patient transmission: blood products

- Major role in the dissemination of HCV until 1990 (in France, 100,000 to 400,000 persons were infected via blood products)
- All the blood products have been incriminated:
 - labile blood fractions
 - stable blood products, including anti-haemophilic factors and immunoglobulins
- By now, the residual risk is very low, estimated to 1 per 12,500,000 transfused units in the 2005-2007 period in France (InVS, 2008)

Indirect patient-to-patient transmission: haemodialysis

High prevalence of anti-HCV antibodies in haemodialysed patients as determined by independent studies performed in different countries:

- 3% in Holland
- 5% in Denmark
- 10% in Germany
- 14% in United-Kingdom
- 15 to 42% in France
- 8 to 50% in USA
- 34% in Slovenia
- 33 to 45% in Tunisia
- 55% in Japan
- 57% in Serbia
- 58% in Italy
- 59% in Taiwan
- 65% in Brazil
- 71% in Kuwait
- 75% in Moldavia

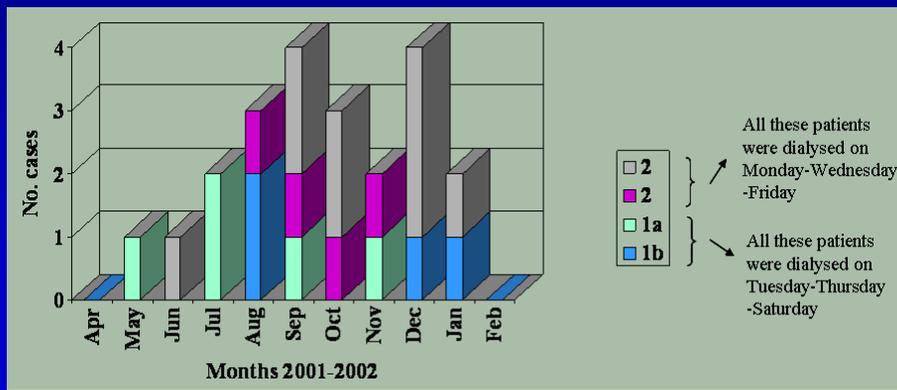
Indirect patient-to-patient transmission: haemodialysis

Annual incidence of HCV contamination in haemodialysis
(Expertise Collective INSERM, 2003)

Author, year	Country	No. centres	Period	No. patients	Annual incidence (%)
Simon, 1994	France	1	1980-1992	217	1.8 to 4.3
Forms, 1997	Spain	1	1991-1995	114	2.3
Jadoul, 1993 & 98	Belgium	15	1991-1995	963	1.41 & 0
Fabrizi, 1998	USA	4	1994-1995	274	0.73
Kobayashi, 1998	Japan	7	1990-1995	179	1
Iwasaki, 2000	Japan	1	1992-1997	142	0.9
Vladutiu, 2000	Roumania	1	1993-1998	180	6.7 to 10.2
Scheeberger, 1998	Holland	34	1997-1998	2286	0.5
Petrosillo, 2000	Italy	58	1997-1998	3926	0.95

Indirect patient-to-patient transmission: haemodialysis

Outbreak of nosocomial HCV infections in an haemodialysis centre, Béziers, France, 2001-2002; 22 patients were contaminated; 4 clones belonging to 3 different genotypes were identified by sequencing (Savey et al., 2003, BEH, 16-17, 104).



Indirect patient-to-patient transmission: haemodialysis

- Modes of contamination (excluding transfusions)
 - cross-contamination via the HCW favoured by:
 - non-respect of standard precautions (as demonstrated by the detection of HCV RNA on the hands of HCW: Alfurayh, 2000, Am J Nephrol, 20, 103)
 - understaffing
 - splashes of contaminated blood from patient to patient
 - sharing of medical devices (i.e. multidose vials)
 - hemodialysis machines
 - role often suspected but never proved
 - possible contamination of the machine via the external filters used to monitor the blood pressure of the patient

Indirect patient-to-patient transmission: haemodialysis

- Preventing measures
 - respect of standard precautions (+++)
 - biological surveillance (the HCV status must be checked by serology and PCR at the entry of a patient in an haemodialysis unit and then in case of ALT increase)
 - signalling new cases to Health authorities
 - reduction of the viral reservoir by treating infected patients
 - isolation?

PROS

Demonstrated efficacy for HBV
No available HCV vaccine
Strategy adapted to each centre:

- geographical isolation
- temporal isolation

CONS

Reduced infectivity of HCV
Lack of sensitivity of serological tests
Risk of superinfection with another virus
Cost

Indirect patient-to-patient transmission: haemodialysis

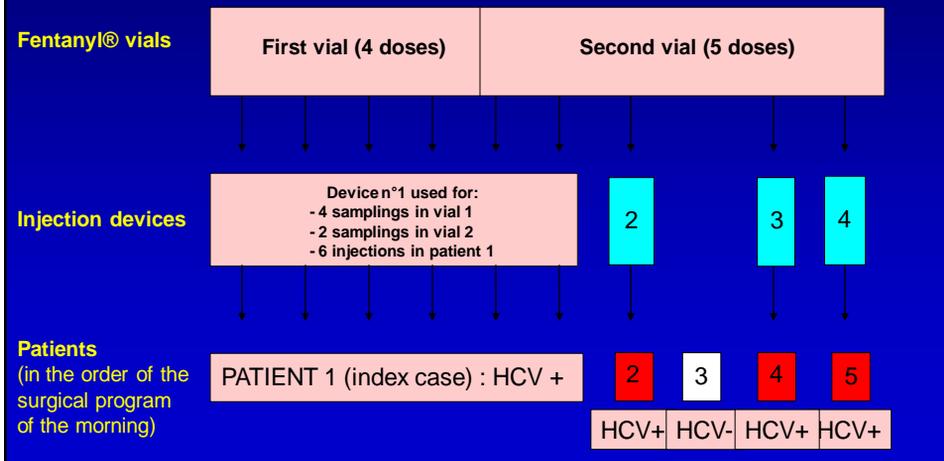
- A study conducted in the hemodialysis unit of a Paris hospital where two cases of HCV seroconversion had occurred, showed that the environment was the probable source of contamination: from 740 surface samplings, 11% showed the presence of hemoglobin and 7% were positive for HCV RNA.
- Girou et al., Clin Infect Dis, 2008, 47, 627-33

Indirect patient-to-patient transmission: other situations

- Mechanism of transmission identified
 - material used for injections
 - in developing countries, the re-use of syringes or needles is probably one of the major route of transmission of HCV (i.e. case of Egypt with a prevalence of 18.1% of infected subjects, mainly with genotype 4 strains, consecutively to the injection of anti-bilharzial drugs between 1920 and 1980)
 - in developed countries, several studies have incriminated the sharing of multidose vials for different patients, one of them being infected by HCV (especially during anaesthesia procedures)

Indirect patient-to-patient transmission: other situations

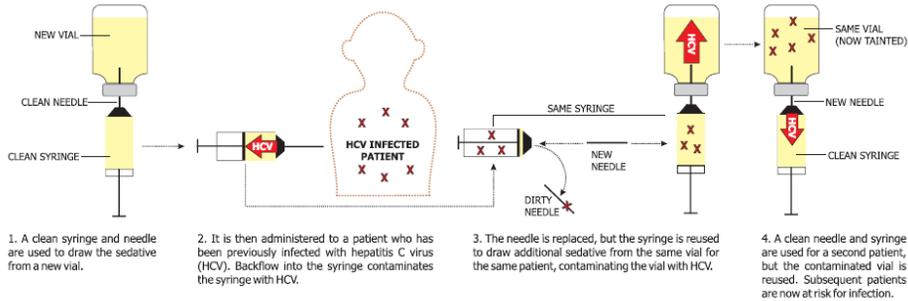
Transmission of HCV by sharing the same vial of anesthetic drug, Eure, France, August 2001 (Germain, 2003, BEH, 16-17, 102)



Transmission of HCV by the multiple use of vials

Unsafe Injection Practices and Disease Transmission

Reuse of syringes combined with the use of single-dose vials for multiple patients undergoing anesthesia can transmit infectious diseases. The syringe does not have to be used on multiple patients for this to occur.



SFAR inquiry, report october 2006
www.sfar.org

**A sample of 1300
anesthesiologists and specialized nurses:
was submitted to an auto-evaluation questionnaire**

Sharing of vials for several patients: never = 81%
Sharing of syringes between several patients: never = 98%
Preparation of syringes at the beginning of the surgical session: never = 52%

Indirect patient-to-patient transmission: digestive endoscopy

2 documented cases of HCV transmission by digestive endoscopy (Bronowicki, J Hepatol, 2006):

- . retro-catheterism of the biliary tract (Tennenbaum, 1993, Gastroenterol Clin Biol, 17, 763)
- . colonoscopy with biopsy (Bronowicki, 1997, NEJM, 337, 237)

suspected mechanism: non-respect of standard precautions or sharing of multidose vials during the anesthesia procedures

Even if the number of declared cases is underestimated and that the number of reported cases is only 1% of observed cases, the risk of transmitting any infectious agent by endoscopy is approximately 100.000 (Nelson & Muscarella, World J Gastroenterol, 2006)

4 case-control studies between 1990 and 2003 in France and Italy: OR comprised between 1.2 and 2.7 for digestive endoscopy

Ciancio et al., Ann. Intern. Med., 2005: no transmission of HCV in a cohort of 8260 subjects having received a digestive endoscopy

Indirect patient-to-patient transmission: other situations

- **Identified mechanism of transmission**
 - 34 children of the same hospital with cystic fibrosis or diabetes infected between 1983 and 1991 by spring-loaded finger stick devices (Désenclos, 2001, ICHE, 22, 701)
 - 43 patients contaminated during vein sclerosis due to the re-use of multidose vials (De Ledinghen, 2005, J Med Virol)
- **Non identified mechanism of transmission**
 - 37 cases of HCV contamination in a Swedish haematology ward between 1990 and 1993 (Allander, 1995, Lancet, 345, 603)
 - 10 patients from a Swedish paediatric oncology ward between 1990 and 1993 (Widell, 1999, Ann Intern Med, 130, 130)
 - transmission of HCV to 2 women during the ancillary procedures for assisted conception (Lesourd, 2000, Hum Reprod, 15, 1083)
 - pharmacological studies (Saginur, 2001, ICHE, 22, 697; Larghi, 2002, Hepatology, 36, 993)...

Indirect patient-to-patient transmission: prevention

- **Respect of standard precautions (++++)**
- **No sharing of devices or vials between multiple patients**
- **Good procedures for endoscope cleaning and disinfection**
- **In some countries, disposable biopsy devices in endoscopy**
- **Regular audit of hygiene procedures for invasive acts**

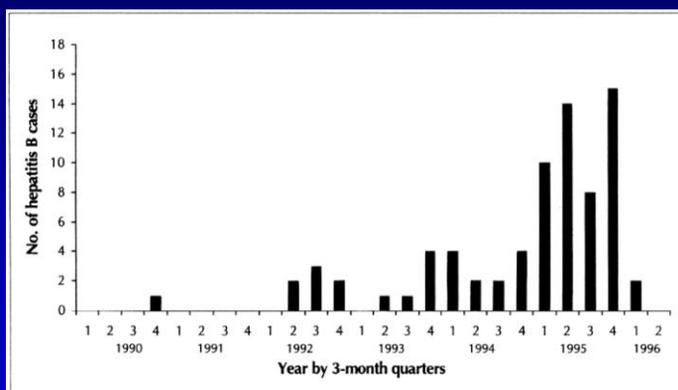
Transmission of blood viruses from health-care workers to patients



Reported cases: HBV

- **December 1994, 42 clusters of HBV transmission concerning 375 patients (GERES report, 2000)**
- **17 publications implying:**
 - 3 orthopedists
 - 3 obstetricians
 - 4 cardio-vascular surgeons
 - 5 other surgical specialties
 - 1 encephalographist
 - 1 acupuncture practitioner
- **At least 37 primary cases and 129 secondary cases**

Index case: encephalographist (technician) positive for HBs Ag of HBV
Number of contaminated patients: 75
Mode of transmission: absence of gloves, hygiene deficiency
Confirmation of some cases by sequencing of a part of gene S



CMAJ 2000;162:1127-1131

Distribution of hepatitis B cases among patients attending electroencephalogram (EEG) clinics in Toronto, Canada, between 1990 and 1996, by date of EEG

Reported cases: HCV

- **11 publications implying:**
 - **2 obstetricians**
 - **2 cardio-vascular surgeons**
 - **1 orthopedist**
 - **3 other surgical specialties**
- **At least 15 primary cases and 5 secondary cases**

HCV

A few case reports involve surgeons or anaesthesiologists:

- England, 1994, **cardiovascular surgery**, one patient (277 tested negative) (Duckworth, 1999, Commun Dis Public Health, 2, 188)
- Spain, 1988-1994, **cardiovascular surgery**, 5 patients (216 tested negative, 1 infected with another strain) (Esteban, 1996, NEJM, 334, 555)
- England, 1978-1999, **gynaecological surgery**, 8 patients (nearly 4500 tested negative in 11 hospitals) (Anonymous, Commun Dis Rep Wkly, 1999, 9, 387 & 2000, 10, 125)
- Germany, 1999-2000, **orthopaedic surgery**, 1 patient (204 tested negative, 2 infected with another strain) (Ross, 2002, J Med Virol, 66, 461)
- Germany, 1993-2000, **gynaecological surgery**, 1 patient (2279 tested negative, 7 infected with another strain) (Ross, 2002, Arch Intern Med, 162, 805)
- USA, 2002, **anaesthesia** for thoracotomy by a physician with acute hepatitis C, 1 patient (348 tested negative) (Cody, 2002, Arch Intern Med, 162, 345)
- England, 2 look-back studies (Pugliese, 2000, ICHE, 21, 619):
 - 1900 patients operated by the same surgeon: 3 were infected
 - 750 patients operated by the same surgeon: 1 was infected

HCV

Other “anecdotal” cases:

- Transmission of HCV by an **anaesthetist assistant** (himself infected by a patient) to 5 other patients during the course of 3 weeks. The transmission occurred through a still weeping finger lesion, favoured by the absence of gloves during cares (Ross, 2000, NEJM, 162, 805)
- Injection of anti-haemophilic factors by an **infected mother** to her child (CDC, 2001, Morb Mortal Wkly Rep, 50, 1)
- **Retired physician** having contaminated a large number of patients with a strain of genotype 5 in the region of Clermont-Ferrand, France. Additional cases were transmitted via blood products of infected patients (Henquell, 2004, J Clin Microbiol, 42, 3030-3)
- **IV-drug abuse HCWs** having contaminated many patients by injecting themselves with the drugs meant for patients:
 - contamination of 171 Spanish patients by an HCW (Bosch, 1998, Lancet, 351, 1415)
 - contamination of at least 9 American patients (Colorado) by a technician assisting surgery (**ProMED alert, July 2009**)
 - contamination of at least 44 Australian women consulting for abortion by an IV-drug abuse anaesthetist, as described above (ProMED alert, May-June 2010)

Reported cases: HIV

- **24 publications implying:**
 - **5 obstetricians**
 - **4 orthopedists**
 - **7 other surgical specialties**
 - **6 dentists**
 - **1 general practitioners**
 - **1 nurse**
- **4 primary cases and 5 secondary cases**

HIV

- **Proven or suspected cases:**
 - **an AIDS-affected dentist in Florida, 1990, 6 contaminated patients, mode of transmission not fully elucidated (CDC, MMWR, 1990, 39, 489 ; Ciesielski et al., Ann Intern Med, 1992, 116, 798 ; Ou et al, Science, 1992, 256, 1165)**
 - **an AIDS-affected orthopedist surgeon, hospital of St Germain-en-Laye, 1992-3, 1 contaminated patient after hip replacement (3 interventions); 3004 recalled subjects, 967 tested (1329 interventions); no additional cases (Lot et al., Ann Intern Med, 1999, 130, 1 ; Blanchard et al., J Virol, 1998, 72, 4537)**

HIV

- **a nurse co-infected by HIV and HCV, 1996, Noisy-le-Sec**
61 year-old female patient with hysterectomy
7580 exposed patients
2293 tested for HIV: no additional case
2215 tested for HCV: 43 positive (1.9%)
(Goujon et al, J Virol, 2000, 74, 2525; Astagneau et al., Am J Infect Control, 2002, 30, 242)
- **an obstetrician from Barcelona, 2003**
female patient with cesarean, neonate not infected
250 exposed women tested negative for HIV
(Bosch, Lancet Infect Dis, 2003, 3, 261)

Relative risk in surgery

- **HBV: HBe Ag +**
 - 0.24 to 0.024 for 100 interventions
 - 1 cases out of 417 to 4167 interventions
 - ref. CDC
- **HCV: HCV RNA +**
 - 0.014 +/- 0.002 for 100 interventions
 - ref. Ross et al, Arch Int Med, 2000
- **HIV: + serology**
 - 0.0024 to 0.00024 for 100 interventions; ref. CDC
 - 0.00768 for 100 interventions; ref. Philips et al., JAMA, 1994

Estimation of the probability of occurrence of some events in health care

Event	Risk for 1 M
Infection by HBV after an exposure to HBe Ag positive blood	300 000
Infection of the surgical site (high risk patient and procedure)	147 000
Infection of the surgical site (low risk patient and procedure)	10 000
Transmission of HIV after an exposure to HIV positive blood	3 000
Transmission of HBV after an intervention by an HBe Ag positive surgeon	240 – 2 400
Mortality associated to anesthesia	100
Aplasia after treatment by chloramphénicol	25 – 40
Transmission of HIV after blood transfusion in USA	6.7 – 25
Mortality associated to an anaphylactic reaction to penicillin	10 – 20
Transmission of HIV after an intervention by an HIV-positive surgeon	2.4 – 24
Death due to an HBV infection after an intervention by an HBe Ag positive surgeon	2.6 – 52.8

Recommandations in France

- **Four axes of prevention:**
 - reduction of the risk of blood exposure
 - screening of at-risk HCWs
 - well-defined strategy for at-risk HCWs or HCW candidates
 - information of exposed patients

Reduction of the risk of blood exposure

- **General measures**
 - standard precautions
 - utilisation of safety material
 - mandatory vaccination against HBV and follow-up by Occupational Medicine
- **Specific measures in the surgical theatre**
 - needle-holder
 - double gloves or special gloves
 - non-coring needles and scissors
 - care management
 - declaration and follow-up of blood-exposure accidents
 - regular evaluation of procedures and of circumstances of blood-exposure accidents

Screening of at-risk HCWs

- **No systematic screening in France**
 - the cost-benefit balance is not favorable
 - the risk evaluation is not possible in the absence of systematic screening of patients
 - the periodicity of screening would be difficult to determine
- **BUT strong incitation to self-screening, notably in case of blood-exposure accident (BEA) and in case of high-risk activity (in the absence of BEA, an annual testing is at least recommended)**

Well-defined strategy for at-risk HCWs or HCW candidates (1)

- **Chronic carrier of HBe Ag**
 - for HCW candidates, judicious choice of the professional orientation
 - for HCW detected positive in the course of his/her job:
 - in case of frequent invasive acts, the professional orientation can be discussed by a specialized commission
 - an antiviral treatment must be discussed in the light of the viral load
- **Vaccine not responder**
 - for HCW candidates, judicious choice of the professional orientation
 - for HCW detected positive in the course of his/her job, annual checking of HBV status

Well-defined strategy for at-risk HCWs or HCW candidates (2)

- **Chronic carrier of HCV RNA**
 - attempt to cure the infection by an adapted treatment
 - in case of non-successful treatment
 - for HCW candidates, judicious choice of the professional orientation
 - for HCW detected positive in the course of his/her job and realizing frequent invasive acts, the professional orientation must be discussed by a specialized commission
- **HCW seropositive for HIV**
 - for HCW candidates, judicious choice of the professional orientation
 - for HCW detected positive in the course of his/her job:
 - no systematic exclusion measure
 - strong recommendation for an efficient tri-therapy conducting to a negative viral load
 - discuss the professional aptitude in the light of the clinical stage (AIDS HCWs must be excluded from at-risk cares)

Information of exposed patients

- **No *a priori* information (by contrast to USA and GB where it is strongly recommended), even if this attitude is contradictory with the principle of patient information about nosocomial and iatrogenic risks (law of March 4th 2002)**
- ***A posteriori* information (recalls of exposed patients) to be modulated according to the benefit-risk balance**

Transmission of arboviruses in relation with labile blood products

**West Nile virus (WNV)
Chikungunya virus (CHIKV)
Dengue virus (DEN-V)**

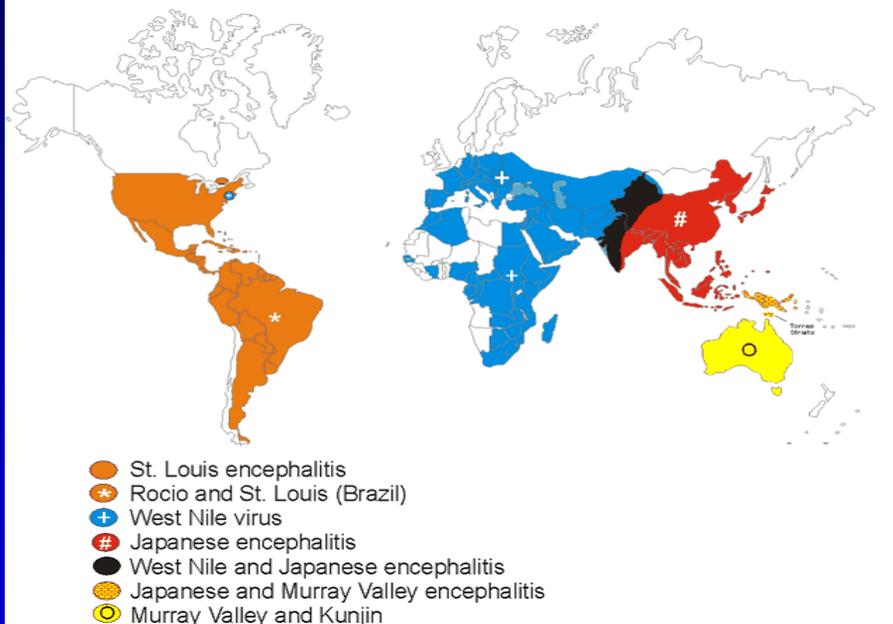
WEST NILE VIRUS



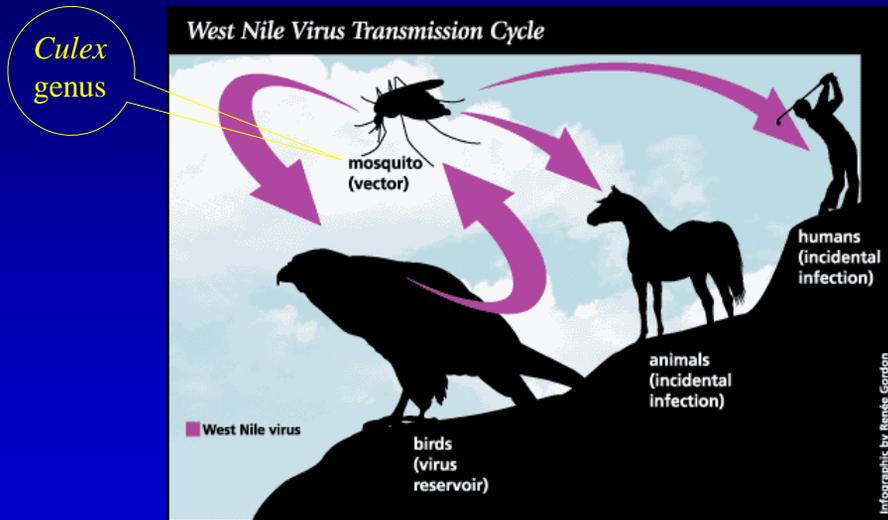
West Nile Virus (WNV)

- *ArBoVirus (Arthropod-born virus)*
- *Flaviviridae* family
- *Flavivirus* genus
- Member of the "*Japanese Encephalitis Antigenic complex*"
 - Japanese Encephalitis virus
 - Murray Valley Encephalitis virus
 - Saint Louis Encephalitis virus
 - Kunjin virus
 - Rocio virus

The Geographic Distribution of the Japanese Encephalitis Serocomplex of the Family Flaviridae, 2000.



West Nile Virus: epidemiology



Nord-american outbreak of WNV (1)

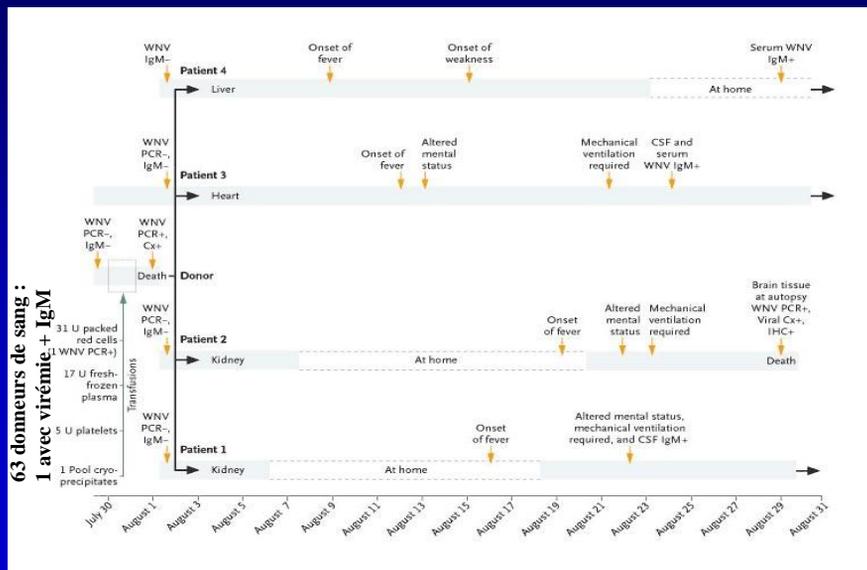
- Occurrence of cases of encephalitis in 1999 summer in New York city
- Particular features of the outbreak:
 - first outbreak due to WNV in the new world
 - high mortality in birds
 - high morbidity in humans: 1 meningitis (1/3) or 1 encephalitis (2/3) for 150 biological infections
 - high mortality in humans: 12% of hospitalized patients

Nord-american outbreak of WNV (4)

- Occurrence in summer and autumn:
 - from 1999 to November 2002:
 - 3495 cases and 204 deaths in USA
 - in 2003:
 - 9862 cases and 264 deaths in USA
 - 1388 cases and 14 deaths in Canada
 - in 2004:
 - 2539 cases and 100 deaths in USA
 - 22 cases and 0 deaths in Canada
 - in 2005:
 - 3000 cases and 119 deaths in USA
 - 224 cases and 12 deaths in Canada

Transfusional cases (1)

Report in August 2002 by the CDC of 4 cases of WNV infection probably transmitted by organ grafts and transfusion of blood products (Iwamoto et al., NEJM, 2003, 348, 2196-203)



Transfusionnal cases (2)

- **Between August and November 2002, 33 cases from 17 american states were reported to CDC as possibly linked to transfusion of labile blood products**
- **6 of them were deeply investigated and led to the conclusion that they were probably linked to the transfusion of blood products**

Measures taken in USA

- **Exclusion of confirmed cases 14 days after the recovery or 28 days after the end of clinical symptoms**
- **Exclusion of suspected cases (unexplained febrile illness) for the same period**
- **Incitation to declare symptoms in endemic areas**
- **Retrospective report of cases in donors**
- **Removal of labile blood products from donors identified as confirmed or suspected cases**
- **Set-up of viral genome diagnosis in July 2003 (sensitivity of 6 to 10 copies/ml):**
 - **Chiron Proteix WNV assay (minipools of 16): 80% USA**
 - **Roche TaqScreen WNV assay (minipools of 6): 20% USA and Canada**

EPIDEMIOLOGY USA 2003

Kleinman et al., Transfusion, 2005, 45, 469-9

- **From July 1st to October 31 2003 :**
 - 2.51 millions of tested donors
 - 877 rejected samples, including 498 confirmed
 - 523 by minipools (384 confirmed)
 - 354 by individual testing (46 confirmed)
 - 3.5 / 10000 blood products (peak to 6.2 in August)
- **Extrapolation for the whole year:**
 - app. 1000 presumed infected donors
 - app. 1500 potentially contaminated blood products

EPIDEMIOLOGY USA 2003-2004

Stramer et al., 2005, NEJM, 353, 451-9

- **Retrospective analysis of results from the American Red Cross 2003-2004:**
 - testing in minipools
 - individual testing in regions exhibiting high incidence
 - 540 positive products in 2003-2004 including 362 (67%) without IgM antibodies
- **148 products (27%) detected only by individual testing, including 15 (10%) without IgM antibodies**
- **Global incidence of positivity during the epidemic periods:**
 - 1.49 for 10000 products in 2003
 - 0.44 for 10000 products in 2004 (half of them coming from 4 counties of South California)

Cost-efficacy studies 2006

«Discussing mass infectious disease screening measures without considering economic consequences is like eating at a smorgasbord without considering calories and fat.»



*B.L. Lee & B.J. Biggerstaff
Plos Medicine, 2006, 3, 168-9*

This relatively cost-efficient strategy at the beginning of the outbreak (incidence of positive samples: 1.5 / 10000 in 2003, 0.44 / 10000 in 2004), is now discussed because of the endemic situation of the WNV infection.

The cost of a one-year saved life, adjusted on the quality of life (QALY) was evaluated to 1.5 million of dollars (Korves et al, Plos Med, 2006, 3, 211-21).

Chikungunya virus



Chikungunya virus

- Chikungunya means « that which bends up » in Makonde language
- Arbovirus from the *Togaviridae* family, *Alphavirus* genus
- Endemic in Africa and Asia
- Transmission by mosquitoes from the genus *Aedes*: *Stegomyia aegypti*, *albopictus*, *polynesiense*...)

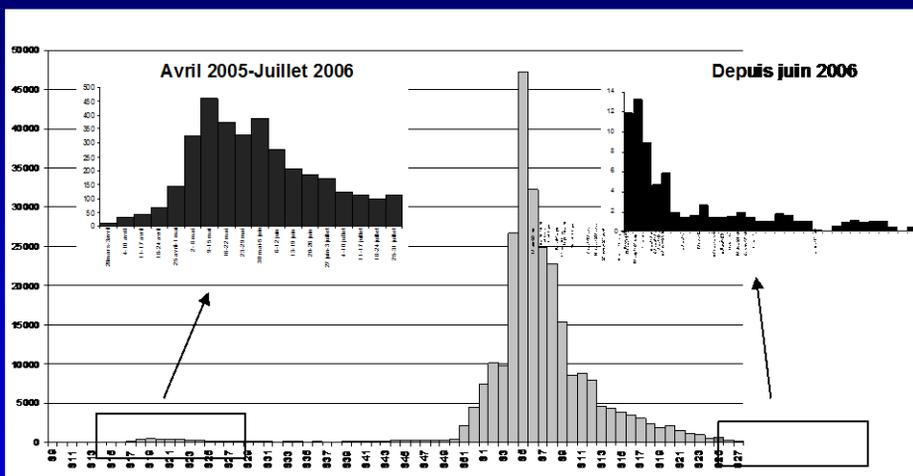
Clinical picture

- Sudden fever with arthralgia
- Frequently associated with myalgia, edemas, rash
- Spontaneous recovery without complications in most cases
- Severe arthralgia for a long time in some cases
- Symptomatic treatment
- Diagnosis by serology (IgM antibodies at day 5), PCR, cell culture

Chikungunya in Reunion island 2005-2006

- Beginning of the outbreak in March 2005
- First peak in May 2005 (450 cases / w)
- 12400 cumulated cases in 2005
- Burst of the outbreak at the beginning of 2006
- 260000 cumulated cases in May 2006 (1200 new cases per week at the peak)
- App. 1/3 of the population got infected

Chikungunya in Reunion island 2005-2006



Suspected transfusional cases in the Reunion outbreak

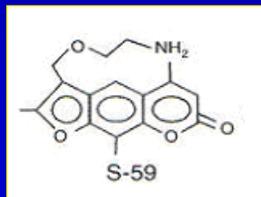
Three suspected cases of Chikungunya virus infection after transfusion of labile blood products during the outbreak
After extensive retrospective analysis, none of them was confirmed

Conservative measures taken by the Reunion blood bank

Importation of RBC from metropolis
Detection of viral genome by PCR testing in local donors
Viral inactivation of platelet concentrates by the Intercept process

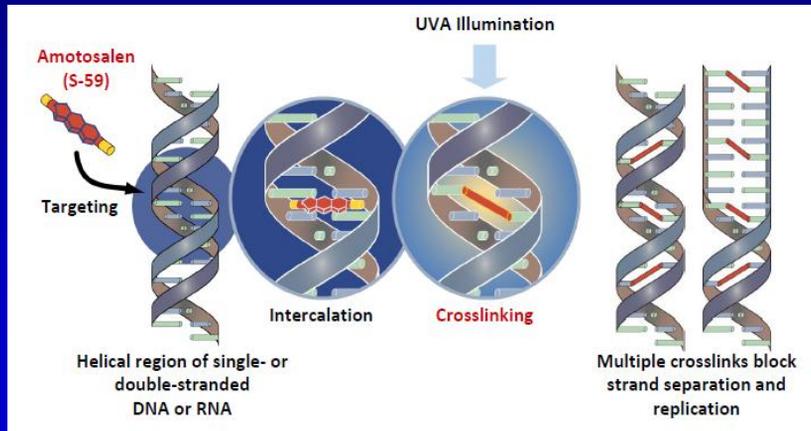
INTERCEPT process (1)

- Process developed by Baxter to inactivate infectious agents in blood products
- Efficacy on enveloped viruses, bacteria, parasites and nucleated cells
- Active compound: psoralene S-59 or Amotosalen



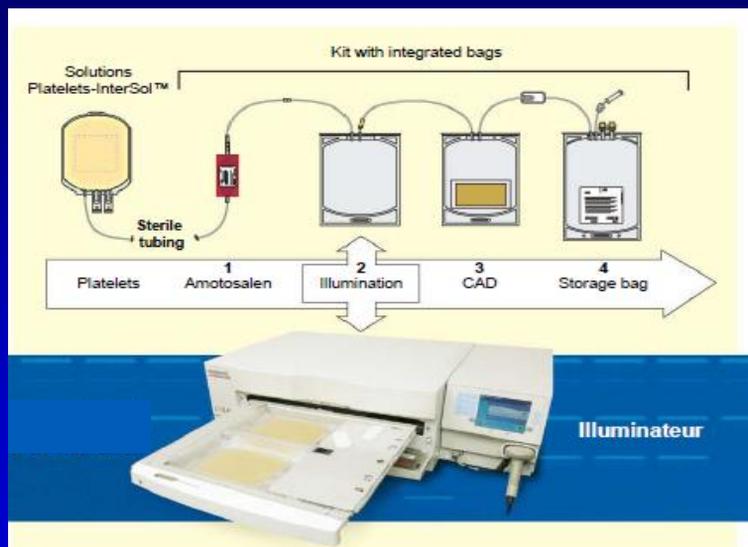
INTERCEPT process (2)

- Mode of action: psoralene S-59 is an intercalating agent that induces irreversible links with pyrimidic bases after UV treatment



INTERCEPT process (3)

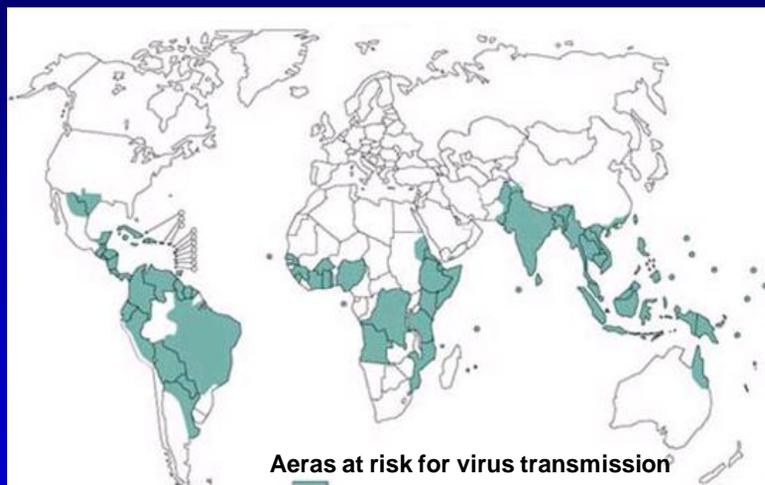
- 5 successive steps:



CHIKV in EUROPE

- In summer 2007, outbreak of 250 cases in Northern Italy following the return from India of a traveler infected by a mosquito bite in this country (Rezza et al, Lancet Infect Dis, 2007, 370, 1840).
- The vector is present along the Mediterranean coasts and notably in the South of France, which creates a favorable situation for the spread of the virus (Circulaire DGS/DUS/RI1/2008/138 du 17 avril 2008 sur le plan anti-dissémination du chikungunya et de la dengue en métropole).
- Two autochthon cases identified in Frejus, Var, in September 2010.

Dengue virus

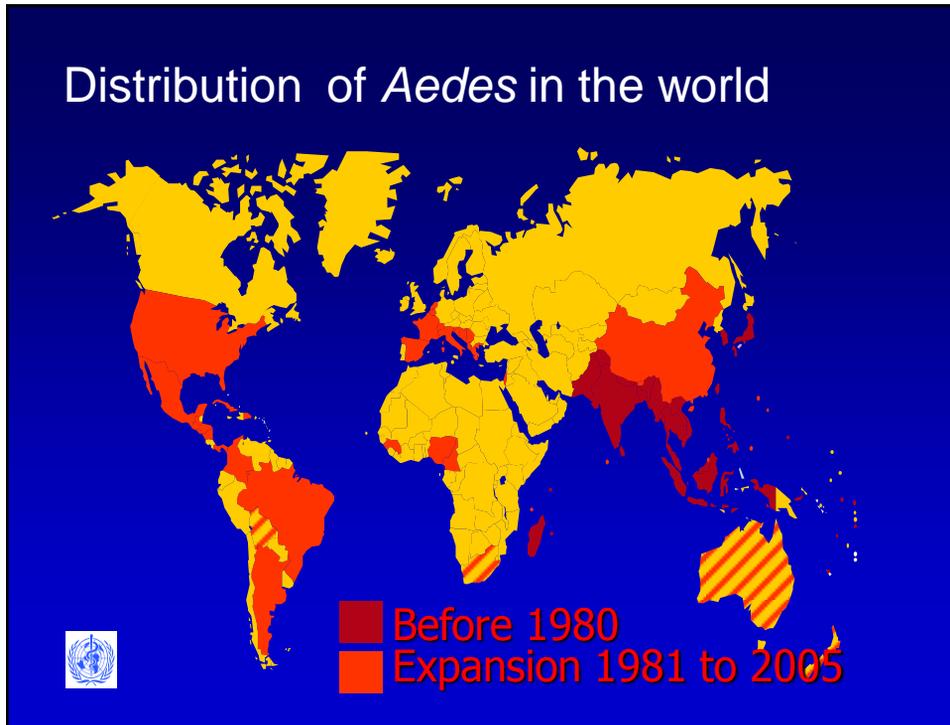


DENGUE VIRUS (DEN-V)

- Main arbovirosis in the world (vector: mosquito of the genus *Aedes*)
- 2.5 billions of exposed subjects in the world
- Tropical and intertropical areas
- *Flaviviridae* family, *Flavivirus* genus
- 4 serotypes: *DEN-1* à *DEN-4*
- Prolonged immunity against one serotype
- Limited cross-immunity between different serotypes

Epidemiological context

- Estimated incidence
 - Dengue: at least 50 millions of annual cases
 - Hemorrhagic dengue: app 500000 annual cases, including 25000 deaths (5%)
- Increase
 - of the area of geographical distribution of the virus and its vector (2 autochthon cases in Nice in 2010)
 - of the number of cases in endemic situation
 - of the number of outbreaks



Clinical picture

- « Common » dengue
 - Very frequent asymptomatic forms
 - Incubation of app. 4-7 days
 - Sudden fever with headache, myalgia, arthralgia, rash, retro-orbital pain
 - Spontaneous recovery without complications in most cases in 8-10 days
- « Hemorrhagic dengue »
 - Described for the first time in Manila in 1953
 - 1-5% of cases
 - Persistent fever with multiple hemorrhages and shock
 - Can lead to death in 1 to 20% of the cases in the absence of rapid treatment in intensive care unit

Transfusional implications

- Two papers in 2008 describing for the first time the transfusional transmission of dengue virus:
 - one case in 2002 in Hong-Kong (Chuang et al, HK Med J, 2008, 14, 170),
 - Another case in 2007 in Singapore (Ehrlich et al., NEJM, 2008, 359, 1526).
- Despite these observations, no specific measures are indicated, except the exclusion from blood donation of subjects with fever.

Transmission of viruses via organ and tissue grafts

HCV
Rabies virus
LCMV

Transmission of viruses via organ and tissue grafts

- **HEPATITIS C VIRUS**
 - Almost all organs and tissues (including cornea) can transmit HCV
 - In most countries, seropositive donors for HCV are excluded (in Spain, kidneys from HCV positive donors are not rejected)
 - Despite serological screening, the risk of transmission is not null (serological window of 2-3 mois)
 - Interest of direct markers (RNA, core antigen)
- **Oregon, USA, oct. 2000 (*MMWR, 2003, 52, 273-6*)**
 - Donor: 40 year-old man, with high blood pressure and habit of alcohol-consumption, who died after stroke
 - Seronegative for HCV, normal transaminases, no skin marks of injection
 - Positive RNA; 1a genotype (tested retrospectively)
 - 91 organs and tissues were taken and 44 of them were grafted to 40 donors (6 organs et 32 tissues)
 - 8 confirmed contaminations (3 organ recipients and 5 tissue recipients);
 - Discovery of the first case in June 2002 (2 years later)

RABIES VIRUS

- **USA, 2005**
- **4 letal cases of post-transplantation rabies:**
 - 2 kidney recipients
 - 1 liver recipient
 - 1 artery recipient
- **Donor died from subarachnoid hemorrhage**
- **Was shown secondarily to have been bitten by a bat**

Srinivasan et al., NEJM, 2005, 352, 1103-11

LYMPHOCYTIC CHORIOMENINGITIS VIRUS

- Arenavirus whose natural reservoir is wild mice and transmitted to man via rodent dejections
- Notification in Massachusetts, April 2008, of two deaths following kidney grafting from a patient infected by the **LYMPHOCYTIC CHORIOMENINGITIS VIRUS** (Barry A et al., MMWR 2008, 57, 799)

**Nosocomial dissemination
of agents of viral
hemorrhagic fevers**

A lot of different viruses and notably:

- Ebola virus
- Marburg virus
- Virus of Lassa fever
- Crimean-Congo fever virus

*(Pozzetto & Berthelot,
HygieneS, 2008)*



Campaign hospital of Médecins sans frontières at Kaluamba, République Démocratique du Congo, in 2008 during an outbreak of Ebola virus



**Treatment room in a Pakistan hospital
where a nosocomial outbreak of
Crimean-Congo fever occurred**

(Fisher-Hoch, Br Med Bull 2005; 73 and 74; 123)

Nosocomial case of VHF in 2008

- Report in July 2008 of the death of a 21 year-old Turkish nurse who worked in the Orthopedic unit of the Bolu hospital, consecutively to an infection by the Crimean-Congo fever virus. This episode is the first reported nosocomial case due to this agent in Turkey (*Yilmaz et al, Eurosurveillance 2008*).
- The Crimean-Congo fever virus, belong to the *Bunyaviridae* family and to the *Nairovirus* genus; it is usually transmitted by tick bite. In 2008, 688 cases of CCFV infection and 41 deaths were recorded in Turkey.



Conclusions

- Many different situations are observed according to the geographic areas and the type of cares
- Very high nosocomial risks are linked to HCV infection
- Some emerging care-associated infections are in relation with climatic and ecologic changes
- Role of healthcare workers as vectors (direct/indirect) as well as victims
- Importance of standard precautions that should allow to prevent most of the nosocomial risks linked to blood exposure
- A careful selection of organ and tissue donors is needed
- Transfusional security must be adapted in accordance to emerging infectious risks