



Editorial

Preventing the transmission of viral hepatitis in the hospital setting

Daniele Prati*

In the absence of donor's screenings, the administration of human blood and its derivatives is a highly effective vehicle of transmission for hepatitis B virus (HBV) and hepatitis C virus (HCV). Clinicians are now facing the consequences of the global epidemics of viral hepatitis emerged in the second half of the 20th century. Several studies have indicated that these epidemics were primarily triggered and maintained iatrogenically by the increasing use of parenteral therapies and blood transfusion (1).

In most rich countries, the rapid and continuous improvement of healthcare conditions and the introduction of laboratory screening for blood donors have led to a dramatic decrease in the incidence of HCV and HBV. Since the introduction of blood donor HBsAg and anti-HCV screening, the residual risk is essentially limited to the units collected during the donors' serological window period (2), although there remains some concern related to the transmissibility of HBV from donors with "occult" infections. Anyway, the risk of developing transfusion transmitted hepatitis has become so small that it cannot be accurately measured by traditional approaches (i.e. prospective surveys of blood recipients) because of the limited number of documented transmission events. It can only be predicted by means of indirect measures,

such as mathematical models involving the incidence of infection and the duration of the pre-seroconversion window period (3). As of the year 2000, the estimates of acquiring HCV were about 1 in 200,000 blood units or less (4 - 6). Just to give a couple of comparisons, this possibility of receiving an HCV-infected transfusion was substantially lower than that of dying after a percutaneous liver biopsy (1 in 10,000 - 12,000) and comparable with that of dying while playing football (1 in 150,000) (1). The theoretical risk of receiving an HBV infected blood unit was approximately 1 in 50,000 units, although the true possibility of acquiring infection was probably much lower because many recipients were either vaccinated or had natural immunity to HBV (4,5). Nevertheless, both the media and the public pushed authorities to add supplemental measures, in the attempt of reaching the "zero risk" for blood transfusion. This led to the introduction, in most European countries, of serological anti-HBc screening, and nucleic acid technology (NAT) testing for HCV RNA and HBV DNA. These measures contributed to a further reduction of the risk of viral hepatitis. Current data indicate that, after HCV-NAT implementation, the theoretical possibility of acquiring HCV infection in USA and Europe ranges between 0.1 and 2 per million units transfused (1). However, it should be considered that overall contribution of HCV-NAT toward reducing the risk of transfusion transmitted hepatitis is marginal, and less than expected in most countries. Of the 58 million donations collected in 14 European countries between 2001 and 2003, only 54 were HCV RNA positive/anti-HCV negative, accounting for a screening yield of 0.93 per million donations (7) as compared to serology alone.

The situation is completely different in developing

* Director of Department of Transfusion Medicine and Hematology,
Ospedale Alessandro Manzoni, Lecco
Postgraduate School of Gastroenterology, University of Milan, Italy.

Correspondence & reprints request: **Daniele Prati**
Director of Department of Transfusion Medicine and Hematology,
Ospedale Alessandro Manzoni, Via dell' Eremo 11/ 92390 Lecco,
Italy.

Phone: (+39) 339 1022840 or +39 0341 489872

Fax +39 0341 489871

Email: d.prati@ospedale.lecco.it

countries. In the poor regions of the world, the sanitary conditions with regards to the prevention of bloodborne infections are comparable to those registered in Europe and USA in the middle of the past century. Blood safety is threatened by a combination of factors due to poverty, including a lack of infrastructures, frequent electricity breakdowns, the unavailability of properly trained professionals, an inadequate supply of instruments and laboratory reagents, and difficulties in mobilising volunteer donors (8 -15)

According to estimates of the World Health Organization (WHO), in the period 2001 - 2002, more than six million blood units were not screened for major blood borne infections, including HCV and HBV. Thirty-one of the 142 developing countries do not undertake any anti-HCV screening, and another 37 screen less than 100% of blood units (9).

To improve this situation, many countries are now allocating economic and organizational resources to improve national blood programs. Libya represents a good example in this field. According to the article published in this issue of the journal by Nuri Dogman and colleagues (16), blood donations are now screened for anti-HCV, anti-HIV and HBsAg by effective immunoassays. To collect additional information with regards to the safety of the Libyan blood supply, the authors examined 100 blood donations for anti-HBc and HCV RNA. The frequency of anti-HBc was 10%. This figure is in the same order of those observed in first time blood donors in Southern Europe, and considerably lower than that observed in Italy before the implementation of mandatory anti-HBV vaccination (17). On the contrary, the frequency of HCV reactivity among anti-HCV negative blood donors was surprisingly high (6%). Such a high prevalence of viremia cannot be explained by the collection of blood donations during the donor window period. The possible causes are sampling errors, and chronic infection by viral variants undetectable by current serological assays. With regards to the first, follow up samples and clinical data from initially HCV RNA positive donors were unfortunately not available; therefore, false positive results can not be excluded. With regards to the second, concerns about the reliability of serological testing in developing countries have been raised in previous reports. Antibody tests for HCV genotypes and subtypes common in Europe and USA might not perform so well with African sera (18,19). In Ecuador, laboratories using rapid tests and certain lots of an enzyme-linked immunosorbent assay

(ELISA) failed to detect HCV reactive sera (20). Studies from China indicate that approximately 1% of seronegative blood units test positive for HCV RNA by RT-PCR (21).

Should Libya join Southern European countries, and recommend additional tests to prevent transfusion transmitted HBV and HCV infection? A definitive answer cannot derive from the interesting and provocative data presented by Dogman and his colleagues, and further analyses are warranted. At a first glance, the introduction of anti-HBc screening would not be sustainable, as it would lead to the elimination of 10% of blood units. With regards to NAT tests, the authors should first confirm the data of HCV viremia in seronegative donations. In case of a confirmation, it will be important to investigate the possible causes leading to false negative results observed by routine immunoassays. In particular, serology protocols should be reviewed, while viral genome sequencing data should be obtained in order to identify possible variants. These analyses will certainly provide the necessary background to decide on further measures to improve the safety of Libyan blood supply. On the other hand, should these preliminary data not replicated, we would have a clear example of the possible disadvantages deriving from the introduction of molecular biology assays in the routine screening of blood donations: besides their high sensitivity, nucleic acid technologies are very prone to give false positive results due to RT-PCR carry over. This may lead to unnecessarily discard blood units, and may ultimately challenge the availability of blood transfusion treatment.

Furthermore, it is now agreed that particularly in countries with limited financial resources the introduction of additional screening assays for blood donations should take into account economical issues. The implementation of NAT tests might have the deleterious effects of shifting resources from related interventions with potentially higher health benefit yields (4), including those aimed at improving the universal infection control standards. In this regard, recent WHO reports indicate the transmission of viral hepatitis through unsafe medical procedures is still a major global health problem. More than 16 billion of potentially unsafe and unnecessary injections are administered annually in the poor regions of the world, and the WHO calculates that they account for at least 10.5 million HBV and HCV new infections per year, 1.2 million premature deaths, and 23.3 million years of life lost due to the complications of these viral infections (22). Campaigns and procedures

aimed at banning the re-use of disposable medical devices, avoid unnecessary injections, and promoting effective sterilization procedures and anti-HBV vaccination, are therefore of key importance in reducing the spread of blood borne infections among hospitalised patients (1,22,23).

In conclusion, the paper by Dogman and his colleagues gives us good news on the fight to viral hepatitis in Libya. We knew from their work that the Libyan blood supply is routinely screened for major blood borne viruses by means of serological assays, and experimental studies are being conducted to monitor its safety. However, it is important that the same attention is paid to reinforce the barriers against patient to patient transmission through non-transfusional routes. We will be able to stop the global epidemic of viral hepatitis only through prudent and concerted interventions.

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