SPECIAL PROBLEMS OF HAEMOVIGILANCE IN THE OBSTETRICAL WARD AND IN THE DELIVERY ROOM

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The problems of haemovigilance in obstetrics largely coincide with the **general** problems of haemovigilance common to the whole of clinical medicine, offering however **a few peculiar aspects** at delivery and in neonatal care, deserving a particular attention (64, 73), which hasn't so far been given with sufficient care to allow any definite conclusions. **Specific data on obstetrical and neonatal haemovigilance** are in fact quite rare in the abundant literature on haemovigilance (28, 36, 44, 59, 64, 70, 73, 76, 78) .

General aspects of haemovigilance

Haemovigilance is receiving an **increasing professional and political attention** in the last years. The Council of Europe, in its *"Guide to the preparation, use and quality assurance of blood components"* (23) (which can be considered by now a "gold standard" for Blood Transfusion Services), has dedicated a chapter to haemovigilance.

In the **European Union Directive** *"setting standards of quality and safety for the collection, testing, processing, storage and distribution of human blood and blood components"* (26), prescriptions are given to member States *(in Chapter V)* to ensure adequate traceability *(Art. 14)* and notification of serious adverse events and reactions *(Art. 15)*, having foreseen *(Art. 29)* the preparation of technical requirements and their adaptation to technical and scientific progress (84) .

Since its first definition (France, 1991), **national** systems of haemovigilance have been implemented in France (since 1993) and in Great Britain, Greece, Switzerland, Ireland, Luxembourg, The Netherlands, Denmark and Sweden (27, 34, 58, 83, 85, 87). **Local** systems of haemovigilance (regional- or hospital-based) are existing in many other European countries (10, 18, 19, 27, 33, 37, 46, 47, 67, 86).

After specific sessions during its European Congress of Venezia *(1995)* (86) and Frankfurt *(1997)* (67), the ISBT is keeping a keen scientific interest in haemovigilance, that has been again debated at the last ***ISBT European Regional Congress*** in Turkey (Istanbul) in July 2003.

Originally hosted by France (Bordeaux, 1997; Lyon, 1998; Lille, 1999; Montpellier, 2000), the annual ***European Haemovigilance Seminar*** has taken place in December 2001 in Greece (Athens), in February 2003 in Amsterdam (The Netherlands), in February 2004 in Zürich (Switzerland), the next being foreseen in 2005 in London (Great Britain).

In 1998, thanks to the initiative of 5 countries of the European Union (Belgium, France, Luxembourg, Portugal, The Netherlands), the ***"European Haemovigilance Network" (EHN)*** was born, having among its aims to allow rapid and efficient exchange of reliable information and experience (website: http://www.ehn-org.net) (33, 85, 87).

Basic requirements for haemovigilance

A satisfactory development of haemovigilance certainly requires the **previous** fulfilment of a series of very simple **requirements,** concerning **basic** clinical care and hospital organisation (7, 10, 33, 68, 71), of which the **European Haemovigilance Network (EHN)** is currently taking care.

These basic requirements have been increasingly debated recently during **ESTM courses,** first in Sofia (Bulgaria, 27/11-1/12/2002) (87), then in Portorož (Slovenia, 12-14/12/2002) (44), Piacenza (Italy, 20-21/6/2003) (85) and Barcelona (Spain, 19-21/3/2004) (46).

In the course of **Sofia** (the **second "Balkan-European" course,** after the good success of the **first** course in 2001 in **Sarajevo** (3) and of the subsequent **work-meeting of June 2002 in Lecce** (72), representatives from all South-Eastern European countries convened, reported their national situation (2, 5, 6, 31, 37, 52, 53, 58, 60, 62, 79, 91) and discussed about basic problems of **clinical transfusion practice** in the view to reach a better **blood safety** (19, 30, 47, 80). The issues dealt with during the course, as necessary **prerequisites** for an effective haemovigilance, did mainly concern the proper **clinical use of blood** and the **hospital transfusion organisation,** following the Directives and Recommendations of the WHO (97, 98) and of the Council of Europe (21, 22, 23). The course was organised in **6** consecutive **sessions:**

- Haemovigilance in Europe;
- Haemovigilance and the Blood Transfusion Service;
- Haemovigilance in the clinical administration of blood;
- Haemovigilance in the countries of South-Eastern Europe;
- "Preventive" haemovigilance: Good Clinical Transfusion Practice;
- Special problems of haemovigilance.

A similar structure characterised the course of **Piacenza** (85), while the programme of **Portorož** (44) also included some data on haemovigilance in Neonatology and Paediatrics (64, 73), and in **Barcelona** (46) the different types of adverse reactions were discussed in detail (18).

Basic professional and political requirements for an effective haemovigilance

An absolutely essential requirement is that a **preliminary consensus** should be obtained from people working in the field, through scientific information, national and European consensus conferences, discussions in ISBT Congresses (as in Venezia (86) in 1995, in Frankfurt (67) in 1997 and in Istanbul in 2003) and in the recent ESTM courses (16, 27, 34, 44, 85, 87).

The **overall evidence** so far arising from the experience acquired in Europe can be summarised as follows (27, 67, 68, 69, 84, 93):

1) Many dispositions, initiatives and organizations **already** exist at national levels, born from very different legal or professional situations, that need to be carefully known and analysed, to limit the tasks of the establishment of an **European haemovigilance network** to the intrinsic proper ones implied by the very word, connecting different settings by a really adaptable modular communication system, avoiding at any rate the risk of creating or imposing a different solution wherever it is already well functioning.

2) For any project of European network to be "feasible", besides its cost and architecture, an essential prerequisite is to be **acceptable** and easy to implement. For any **implementation,** most of all considering the wide variations in the development of blood transfusion systems existing in Europe, a **preliminary consensus** from the people working in the field (i.e. from the experience of most European National Societies) seems to be essential.

3) Considering the increasing political need of reassuring the public about "adverse events" of blood transfusion being under full control (unfortunately corresponding to a lack of attention on its beneficial effects!), one should absolutely avoid the **risk** that the incoming European legislation on haemovigilance be characterised by an excessive prevalence of "bureaucratic" and over-regulatory aspects, dictated by mostly **legal** precautions, rather than by a strict adherence to the **scientific** and **medical** contents of our profession.

Basic clinical and organisational requirements for an effective haemovigilance

(4, 10, 32, 33, 68, 74, 85, 87)

Specific **tasks** necessary for the implementation of the surveillance of transfusion therapy in hospitals and clinical departments are:

- Definition of basic laboratory and clinical **indications** for the transfusion of blood products.
- System of **ordering** blood products and standardized forms for their request and forms that accompany them. This system must define labels, that have to be put on blood products that have been prepared for the transfusion of a defined patient, and labels that have to be put on withdrawn or recalled blood products.
- Unique **identification** system for the patient, blood product and laboratory results.
- **Collection** of patient blood **samples** and their labelling.
- **Transport** of requests and blood **samples** to the Blood Transfusion Centre.
- **Transport** of blood **products** from the Blood Transfusion Centre to the clinical departments.
- Temporary **storage** of blood products in the required conditions in the clinical departments until they are transfused, or if they are not used, until they are returned to the Transfusion Centre, and responsibility for them.
- **Identification** of the patient and blood product immediately before the transfusion, and comparison of the data obtained from the patient with the data on the blood product and with the results of laboratory testing that are written in the form accompanying the blood product.
- **Monitoring** the transfusion process. Although it is not realistic to expect it to be routinely done, the long-term monitoring of the transfused patient would give us much more information about the outcome of transfusion therapy.
- Documentation of transfusion and its outcome in the **patient medical file.**
- **Report** of the **outcome** of each transfused unit and of the monitoring of each transfusion event.
- The **alert system** involves recording the occurring of adverse events, measuring their prevalence and characteristics, notifying the Blood Transfusion Centre (and with their assistance withdrawal or recall of all blood

products produced from the same donor), and notifying other institutions that are mandatory or necessary for prevention of adverse reactions in other patients.

- Return of every **empty blood product bag** after the completion of every transfusion or of every **nontransfused blood product** to the Blood Transfusion Centre.
- Monitoring documentation of **patients state** before and after the end of transfusion, or regularly at defined times during transfusion therapy (general state, blood pressure, frequency of heart beat).
- Documentation of the **blood product.**
- Documentation of the **medical person,** who performed the procedure and was responsible for it, in the patient's file.
- Documentation of each **adverse event** that occurred during or after the transfusion therapy in the patient's file.
- Collection of data on adverse reactions, and analysis, by hospital **Transfusion Committee.**

Special problems of haemovigilance in obstetrics and neonatology

While **haemovigilance basic rules** are very much the **same** for pregnant women needing transfusion as for any other adult patients (what documentation, traceability and adverse event reporting concerns) (11, 12), **special attention** should be paid to what happens in obstetrical **emergencies,** in **autologous** transfusion, in **"mother-child" situations** (as transfusion of pregnant women, intrauterine transfusion and immunoprophylaxis of HDN with anti-D Ig), and in **newborns** (who are often kept under obstetrical medical care and assistance in the first hours or days of life).

Haemovigilance in obstetrical emergencies

As in any other kind of emergency in clinical medicine, detailed and complete **protocols** should be in place, concerning **all steps** to be done, well known and normally followed by **all staff** involved in emergency situations.
The need for such protocols is mostly evident:

1) for **blood component** request, preparation and administration (39, 47, 80), and
2) for diagnosis of **haemostatic** emergencies possibly requiring urgent selective transfusion therapy (38, 39).

Documentation of any transfused blood component unit should never be omitted in any emergency, not only during **pregnancy,** but as well at **delivery.**

Haemovigilance in autologous transfusion

The incidence of adverse events associated with **autologous** donation in the general patients' population has been estimated as approximately 2,6% (35) and seems therefore to be **under-reported** to SHOT (77), where only 3 cases are quoted. In the Irish NHO Annual Report 2003 (51), pre-deposit autologous donation accounts for 3,3% of the total incidents reported (6 out of 180).

In spite of the obvious fact that its inherent immunological and virological **advantages** would concern also the **fetus** (9), autotransfusion is very **seldom practiced** during pregnancy and should be planned, (under the responsibilities

of the attending physician) in the last 3 months of pregnancy only as a **precautionary measure** in women with a predictable **risk of haemorrhage** (placenta previa, previous caesarean delivery, multiple pregnancy) or with a **rare blood group** (9, 40, 41, 45, 54, 61, 63).

In such cases, **all steps** involved need to be completely **documented** with particular care, also considering the relative lack of regulations and protocols about autologous transfusion (15, 49, 77, 80), which holds the same risks as allogenic transfusion in terms of bacterial contamination and identification errors at the time of administration (49, 50).

It may be of interest to know that in the next 11th edition (2005) of the Council of Europe's Guide, at page 55 under *"Conditions leading to temporary deferral"*, a statement shall be reintroduced concerning conditions for **normal** homologous blood **donation** in relation to **pregnancy**, such as ***"6 months after delivery or termination, except in exceptional circumstances and at the discretion of a physician"*** (88).

Haemovigilance in "mother-child" situations

In a recent discussion by Weiller and Coll. (95), referring to the rather complete series of prescriptions and guidelines existing in France on haemovigilance in paediatric transfusion, a **mother-child link on the transfusion file** has been recommended (also for intrauterine transfusions) and a definition of the **immunohaematological and virological follow-up in children having been transfused in the neonatal period** has been advocated.

Traceability between mother and child is much too often made difficult or impossible by the lack of necessary **documentation,** that should never be omitted on **both** (mother **and** child) separate clinical **and** transfusional **files,** in the following **"mother-child" events** (95):

1) **children** transfused **in utero**;
2) **children** whose mother has been transfused **during pregnancy**;
3) **mothers** whose child has been transfused **in utero**.

In all these cases the immunological and infectious **risks** concern potentially both mothers **and** child, irrespective of which is being **"directly"** transfused.

It is astonishing how often it is acritically accepted that the **fetus** and the **newborn** have no **own identity**, but only with reference to the mother.

Documents with previous (mother-mediated or direct) **transfusion history** of **neonates** are seldom drawn up and given to the families. As a result, most adults completely **ignore** their neonatal (and/or fetal) transfusion history, making traceability, looking-back and follow-up procedures impossible.

It is our impression that an increased sensitivity to the need of **reliable "mother-child" clinical and transfusion files** would greatly increase the possibility for haemovigilance to help improve obstetrical and paediatric care.

Transfusion of pregnant women

Children whose mothers have been **transfused during pregnancy** are certainly the great majority of cases with **undocumented** exposure to previous immunological and/or infectious risk.

A **"neonatal" transfusion file** (with data of all transfusions received by the mother during pregnancy) would be particularly useful in cases of **chronic hereditary haemolytic anaemias** (thalassaemia major, sickle-cell syndromes), where also "prophylactic" transfusions may be indicated (89).

Intrauterine transfusion

Three IBCT errors reported in the SHOT Annual Report 2001/2002 (76) concerned babies who were given non irradiated blood, being the laboratory and medical staff unaware that infants who have had an intrauterine transfusion (IUT) should thereafter receive **irradiated** cellular blood components (14).

Although quite less frequent, one should not forget that **intrauterine transfusion (IUT)** is an event concerning **both** (fetus **and** mother) from an **immunological** and **infectious** point of view.

Immunoprophylaxis of HDN with anti-D Ig

The data reported by the National Haemovigilance Office (NHO) of the **Irish** Blood Transfusion Service (42, 49, 50, 51, 75) on the errors related to **prophylactic anti-D Ig administration** (39 in the period 2001-2003 (42, 75)) open a new perspective on the interest of haemovigilance in regard to Obstetrics.

Out of **11 incidents involving anti-D Ig during 2003,** 6 concerned errors in administration, 1 omission and 4 delays (5-9 days) of administration (50, 51).

Of the **6 errors in administration,** 3 arose from making incorrect assumption rather than checking the patient record (1 to a D-positive mother, 1 to a mother of D-negative child, 1 to an already D-sensitised mother), 1 from an error in cord blood grouping, 1 from a prescription written up for the wrong patient, and 1 from a label with incorrect patient details. Although none of the 6 patients suffered complications from these incidents, 5 of them were unnecessarily exposed to a blood product (51).

Of the **5 errors of omission or delay of administration,** 2 arose in the clinical area (failure to take cord blood samples, lack of awareness of anti-D requirements in a general surgical ward where the patient was nursed), 1 in the laboratory (transcription error of a cord blood group result), and 2 involved the clinical/laboratory interface (telephoned report of result from laboratory to ward, early discharge of mothers after delivery before blood group results were available). All the 5 patients are being presently followed up to exclude sensitisation (51).

The **main general recommendations** arising from the analysis of these 11 incidents are summarised (50, 51) as:

- need of **coordinated approach** to ensure that **decisions** to issue and administer anti-D Ig are based not on assumptions, but on **documented** laboratory results;
- need of **education** of **all staff involved** in prescription/administration of anti-D prophylaxis;
- need of a **linked** (**laboratory-ward**, and **mother-child**) **information system**, to avoid errors or delays due to telephone communication or manual transcription of results;
- formal identification **procedure at bedside** (both at prescribing and administrating anti-D Ig) to check **identity** and **D status** of **mother** and **child.**

Haemovigilance in neonatal transfusion

Incidents reported in **established haemovigilance schemes** are not often related to different ages: data relating to **paediatric** age have only recently started to be separately considered (49, 50, 51, 76, 78) , making a thorough evaluation of **specific** neonatal problems still uneasy.

Data have been reported by Revill (64), extracted from **5 years' activity of SHOT** (from 1996 to 2001) and referring to 88 cases ranging from 0-1 day to 10-18 years of age. Besides 10 cases of acute transfusion reactions (ATR), 7 of TRALI and 2 of TA-GvHD, the great majority (64) were due to **incorrect (or inappropriate) blood components transfused (IBCT)**, among which 44 cases involved children under the age of 6.

The **IBCT causative error** in the above series of paediatric/neonatal patients seemed to differ from the overall SHOT frequency (laboratory 41% versus 28%; collection and administration 25% versus 55%), but the large discrepancy of the number of cases in the 2 series (69 versus 699) may make the difference not statistically significant, and rather stimulate the acquisition of new, larger data (64).

In the **last SHOT report** on transfusion events in patients **less than 18 year** of age (78), the **49%** of cases occurred in infants **less than 1 year** of age, of whom **69%** were in their **1st month** of life. All reported events in this last group (less than 1 month) were IBCT (incorrect blood component transfused).

The above data reflect the relative **high incidence of transfusion in the neonate** because of the complication of prematurity and congenital malformation, and the requirement for special consideration of **blood component selection** in the neonate (78). Given the lack of clear evidence-based criteria for the administration of red cells to neonates (14) it is recommended that local transfusion **protocols** be established for neonates in all hospitals (66).

Two of these IBCT concerned newborns in the **first day** of life. The **first** of them was caused by a **laboratory error**: group A red cells transfused to group A infant (with undiagnosed mild ABO HDN) of group O mother, ensuing severe haemolysis requiring group O exchange-transfusion. The **second** concerned a newborn (who previously had an IUT) exchange-transfused with blood (crossmatched for an IUT) taken (by **error in the ward**) from a satellite refrigerator.

The above cases illustrate the particular attention to be exerted in the **difficult diagnosis of mild ABO HDN**, and the need for clinical staff to be aware of the **specific requirements** for blood for **exchange-transfusion** and **IUT**, both uncommon procedures.

Another case of **error in the ward** is reported (78), where a group A baby requiring transfusion was transfused with (group O-negative compatible) blood crossmatched with another group B baby's mother's sample mistakenly sent from the ward. Although no harm came to this baby, **misidentification** at the time of sampling and administration (verbal identification being impossible) can lead to fatal ABO-incompatible transfusions (14, 78). Wearing and checking of **wrist or ankle name bands** are essential in neonates, being the last opportunity to identify an error arising earlier in the transfusion chain (14, 29).

In the **Irish** Haemovigilance Reports, 5 neonatal out of 12 paediatric cases were reported in 2002 (49), and 4 neonatal out of 26 paediatric cases in 2003 (50, 51).

Small volume neonatal transfusion

Dedicating aliquots from a single donation of red cell to allow sequential transfusions from the **same** donor for an individual neonate who is likely to be **repeatedly** transfused, significantly **reduces exposure** (20, 65, 82, 96) to immunological and infectious risk, and has been **recommended** for small volume transfusions in neonates by the British guidelines (12, 13, 14, 92).

The malpractice of shared neonatal micro-transfusions

Among the medical procedures used in Italy and elsewhere in the 1960ies, a quite **common practice** was to give a few mL of blood or plasma from the same donor to **many** underweight or **pre-term** neonates (81), regarded as "immature" (17) if the birth weight was less than 2.500 g, considering blood transfusion as necessary to correct the inherent anaemia (94).

One could therefore postulate (51, 55, 90) that this practice might have been the **cause of HCV infections** seen today in the fraction (30-50%) of anti-HCV-positive adult individuals with a negative history for any known risk factors (1, 97).

Data from a survey in 2000 by De Paschale and Coll. (24) on the transfusion files of 613 children microtransfused (in the years from 1968 to 1974) with blood or plasma within the first year (of which 494 within the first month) of life have shown evidence that some HCV infections in adults with a negative history of risk factors might be **traced back** to microtransfusions received as neonates or within the first year of life (24).

The results of a previous study (in 1994), on 46 Spanish and Italian children with post-transfusion hepatitis C (8), indicated **that transfusions in the perinatal period** are the **single most important cause of hepatitis C** in otherwise healthy children.

Moreover, given the apparent failure of humoral immune response in cases of neonatally acquired chronic HCV infections (48), an adequate look-back investigation should always include **HCV-RNA testing** also in presently anti-HCV-negative neonatally transfused individuals.

Being all the above findings referred to blood or plasma microtransfusions in a period where no HCV screening was available in Blood Transfusion Services, it is to be expected that the number of post-transfusion cases will have decreased in the subsequent years (8). However, the **malpractice of indiscriminate neonatal microtransfusions**, particularly of **plasma**, hasn't unfortunately completely died out in all European countries and is **not always**, moreover, adequately **recorded on clinical files** (70, 73).

Conclusions

Although the children transfused in the neonatal period of life are long-living survivors of blood transfusion (51, 55), they are the most vulnerable of transfusion recipients, and the **perinatally acquired HCV infection** persists a long time in adult life (57): the practice of sharing donations should therefore be definitely discouraged (54, 55, 70, 73, 90).

While attention has been adequately focused on **red cell** transfusions in neonatal care (25), most neonatal microtransfusions of **plasma** may still pres-

ently (as certainly in the past) remain **unknown** to the recipients, **not** being adequately **documented** in clinical files.

Although most of the transfusion procedures in obstetrics and neonatology are included in the common frame of **general haemovigilance**, we may draw a few **specific** conclusions:

1) "The importance of **good and accurate communication** at every level in transfusion practice, by **all** involved in the transfusion process, must be emphasised to prevent unnecessary error" (29, 78).

2) In Obstetrics and Neonatology, as well as in all other clinical specialities, the **same general rules** of good transfusion practice (65, 97, 98) and of haemovigilance apply.

3) For a haemovigilance system to be effective also in obstetrical and neonatal practice, some **basic clinical** (including correct and evidence-based indications for plasma transfusion! (13, 43, 65)) **and organisational requirements** must be previously fulfilled.

4) A new approach must be started on the need of a separate (mother **and** child) specific **documentation** of **mother-child-linked transfusion events.**

5) The **practice of shared neonatal microtransfusions** represents a ground for some specific measures of good transfusion practice and **neonatal haemovigilance**.

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