3. podiplomski seminar

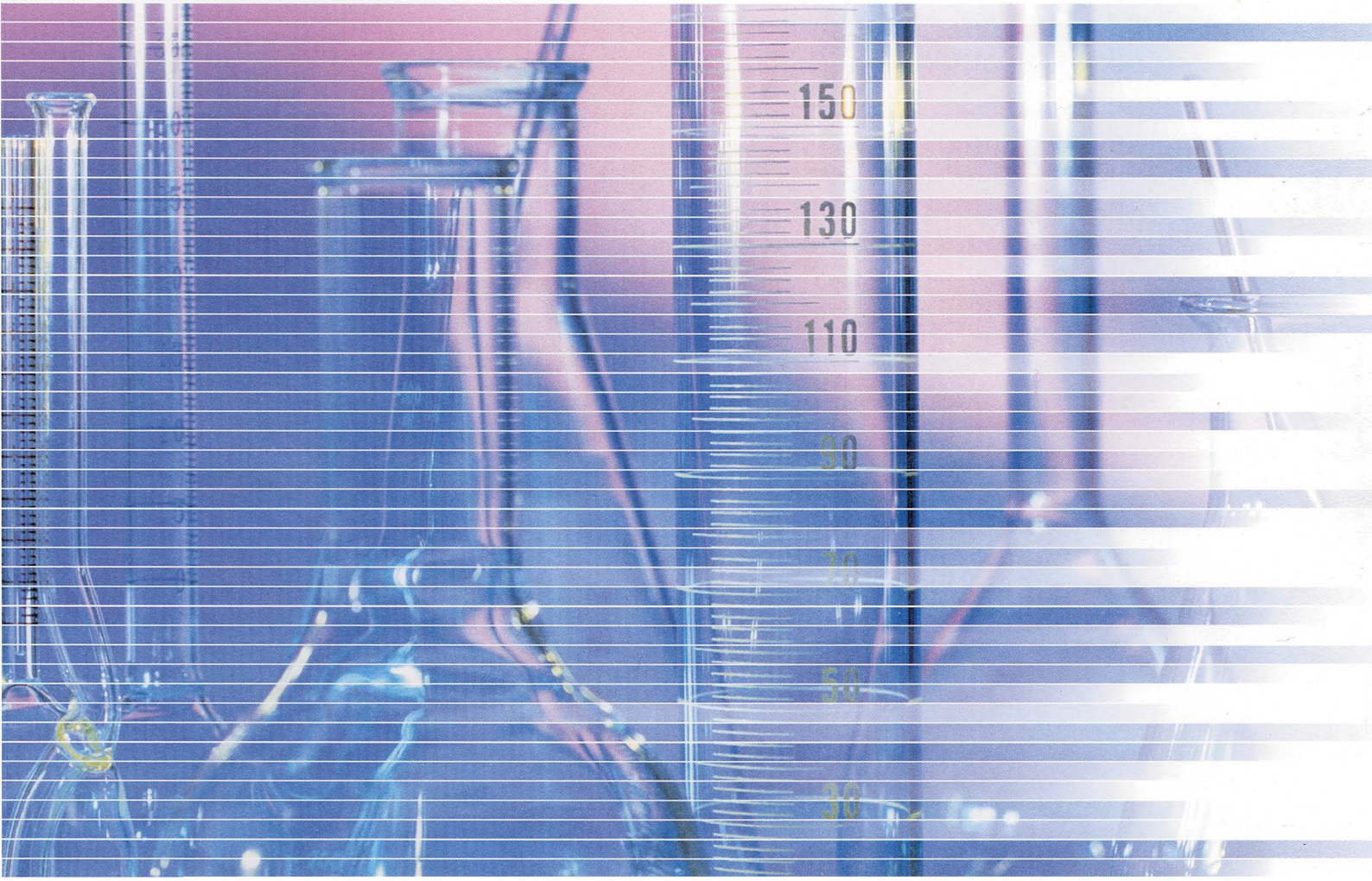
# zdravljenje s krvjo v kirurgiji

## zagotavljanje varnosti

3rd postgraduate course

# blood therapy in surgery

## safety assurance in blood therapy




Portorož, Slovenija, 14. - 16. december 2000

ORGANIZATORJI:

KLINIČNI CENTER LJUBLJANA - SPS KIRURŠKA KLINIKA
UNIVERSITY MEDICAL CENTER - DEPARTMENT OF SURGERY

ZAVOD RS ZA TRANSFUZIJO KRVI
BLOOD TRANSFUSION CENTER OF SLOVENIA

ESTM - EVROPSKA ŠOLA ZA TRANSFUZIJSKO MEDICINO
EUROPEAN SCHOOL OF TRANSFUSION MEDICINE

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Irena Milič

*Kazalo / Index*

**Četrtek, 14. december 2000**

16.00 PRIJAVA
17.00 SESTANEK STROKOVNEGA SVETA *(KOORDINACIJA BOLNIŠNIČNIH KOMITEJEV)*
18.00 OTVORITEV, UVODNO PREDAVANJE - *Voljč B.: Zakon o preskrbi s krvjo*
19.00 SPREJEM

## SKUPNI PROGRAM

**Petek, 15. december 2000**

## TVEGANJE IN VARNOST

*moderatorja:* Rossi U.
Grgičević D.
8.30-9.00 *Barbara J.:* Zmanjšanje tveganja - uskladitev z epidemiologijo
9.00-9.30 *Rossi U.:* Nujnost uskladitve kriterijev in postopkov za zagotavljanje varne krvi v Evropi
9.30-10.00 *Hafner V.:* Varna kri v evropskih državah z omejenimi sredstvi
10.00-10.30 Razprava

10.30-10.45 **Odmor**

*moderatorja:* Rossi U.
Grgičević D.
10.45-11.15 *Barbara J.:* Tveganje zaradi transfuzije in pogled na to tveganje v širšem kontekstu
11.15-11.45 *Grgičević D.:* Upravljanje sistema kakovosti in kontrole kakovosti za zagotavljanje varne krvi
11.45-12.15 *Hafner V.:* Pogledi WHO na varnost krvi
12.15-12.45 Razprava

12.45-14.00 **Kosilo**

*moderatorja:* Arnež Z.
Domanovič D.
14.00-14.20 *Arnež Z.:* Tveganje in varnost kirurškega posega
14.20-14.40 *Eržen-Paver V.:* Tveganje in varnost anestezije
14.40-15.00 *Lukič L.:* Tveganje in varnost transfuzije krvi, krvnih sestavin in zdravil iz krvi
15.00-15.20 *Potočnik M.:* Tveganje in varnost pri navzkrižnem preizkusu
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16.10-16.20 *Domanovič D.:* Hemovigilanca
16.20-16.40 *Černelč P.:* Vloga zdravnika pri postopkih transfuzije krvi
16.40-17.00 *Zupančič P.:* Vloga višje medicinske sestre pri postopkih transfuzije krvi
17.00-17.20 *Balažic J.:* Odgovornost zdravnika in višje medicinske sestre pri transfuziji krvi
17.20-17.40 Razprava

19.00 **Slavnostna večerja**

## UČNE DELAVNICE

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2. Naročanje krvi in dajanje transfuzije
10.00-10.45 *Smit Sibinga C. Th.:* Delo bolnišničnih transfuzijskih odborov - Evropska priporočila

10.45-11.00 **Odmor**

11.00-12.00 SKLEPNA KONFERENCA

**Thursday, 14th December 2000**

16.00 REGISTRATION
17.00 MEETING OF SCIENTIFIC COUNCIL - *COORDINATION OF TRANSFUSION COMMITTEES*
18.00 OPENING CEREMONY AND LECTURE *(Voljč B.: The Legislation on Blood Supply in Slovenia)*
19.00 RECEPTION

## PLENARY SESSIONS

**Friday, 15th December 2000**

## BLOOD SAFETY TODAY

*moderators:* Rossi U.
Grgičević D.
8.30-9.00 *Barbara J.:* Risk reduction: how to reconcile it with epidemiology
9.00-9.30 *Rossi U.:* The urgent need of mutually compatible criteria and behaviour for blood safety in Europe
9.30-10.00 *Hafner V.:* Blood safety in European countries with limited resources
10.00-10.30 Discussion

10.30-10.45 **Coffee break**

*moderators:* Rossi U.
Grgičević D.
10.45-11.15 *Barbara J.:* Transfusion risk and its perception in a wider context
11.15-11.45 *Grgičević D.:* Quality control and quality management of blood safety
11.45-12.15 *Hafner V.:* WHO perspective on blood safety
12.15-12.45 Discussion

12.45-14.00 **Lunch**

*moderators:* Arnež Z.
Domanovič D.
14.00-14.20 *Arnež Z.:* Risk and safety of surgical procedures
14.20-14.40 *Eržen-Paver V.:* Risk and safety of anaesthesia
14.40-15.00 *Lukič L.:* Risk and safety of blood transfusion, blood components and drugs made from blood
15.00-15.20 *Potočnik M.:* Risk and safety of cross-matching
15.20-15.40 Discussion

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## RESPONSIBILITY

*moderators:* Brubnjak Jevtič V.
Lukič L.
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16.10-16.20 *Domanovič D.:* Hemovigilance
16.20-16.40 *Černelč P.:* The role of physicians in blood transfusion
16.40-17.00 *Zupančič P.:* The role of nurses in blood transfusion
17.00-17.20 *Balažic J.:* Responsibility of physicians and nurses in blood transfusion
17.20-17.40 Discussion

19.00 **Gala Dinner**

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9.00-10.00 Workshops and video presentations
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*2.* Ordering blood and administering transfusion
10.00-10.45 *Smit Sibinga C. Th.:* The work of hospital transfusion committees - European guidelines

10.45-11.00 **Coffee break**

11.00-12.00 CLOSING CONFERENCE

# Risk reduction: how to reconcile with epidemiology?

*John Barbara*

## Summary

Throughout Europe the prevalence and incidence of the various agents that are potentially transmissible by blood transfusion can vary from country to country, and there may be significant differences even within a single country. Before one can decide on the value and appropriateness of extra testing for a given marker, the following information needs to be obtained, checked for accuracy, collated nationally, and compared throughout Europe:

1. Prevalence of *confirmed* positivity rates for the markers of transfusion-transmissible infections (TTIs).
2. Carefully evaluated rates of seroconversion to provide data on incidence of these infections in blood donors.
3. Mean inter-donation intervals for regular blood donors.
4. Proportion of new and repeat donors (using agreed definitions within Europe).
5. Calculations of residual risk of the various infections per donation due to ''window-period' infectivity can then be made.
6. Investigation of reported cases of transfusion-associated infections, and collation of the data.

## Surveillance of TTIs in blood donors

A centralised national scheme for the reporting and collation of data on blood donors found to be infected with transfusion-transmissible agents is the first prerequisite for the assessment of microbial risk from blood transfusion. All repeatably reactive donations should be confirmed by appropriate reference testing and only confirmed positive results should be reported to the national register. Data should be subdivided into confirmed positive rates for new donors and for repeat donors. The latter will presumably have been previously negative for a given marker and, if previously tested by an assay of the same sensitivity as when confirmed positive, the result will represent seroconversion subsequent to the previous donation. If the average inter-donation interval for repeat donors is known, estimates of incidence rates can be obtained. When incidence is multiplied by the window-period for a given infection, the residual risk per donation for that agent entering the blood supply can be computed.

When assessing seroconversion it is important to check the following (1a, 1b).

- the donor is indeed a repeat donor, and has previously been tested by an assay of equal sensitivity.
- the reactivities have been confirmed by Reference testing.

Ideally, a stored sample of the previous donation should be tested with reference assays (which may include PCR if appropriate) in parallel with the current sample. To this end, a programme for maintenance of a frozen archive of all blood donation samples (e.g. for 3 years storage) is of obvious value. Seroconversion rates for HCV in England have recently been analysed in detail on the above basis (2).

For new donors positive reactions may reflect prevalent or incident infection, but

seroconversion on the basis of a single sample is not generally determinable. An exception may be for HBV infection if carefully defined algorithms for anti-HBc IgM determination together with liver function testing and donor follow-up are in place. Usually, however, incidence of infection in new donors is estimated by surveying incidence in repeat donors and multiplying this parameter by a factor based on the ration of confirmed positivity rates in new and repeat donors. To this end, cumulative national surveillance of infection rates in blood rates is of great value, as exemplified from English data (courtesy of Kate Soldan) shown in figure 1 (a-b).

Ideally, surveillance following strictly defined rules for case ascertainment should be analysed for the whole of Europe. The European Plasma Fractionation Association (EPFA) currently obtains and collates such data under their own initiative and have recently prompted discussion about standardisation of definitions.

## Calculation of residual risk

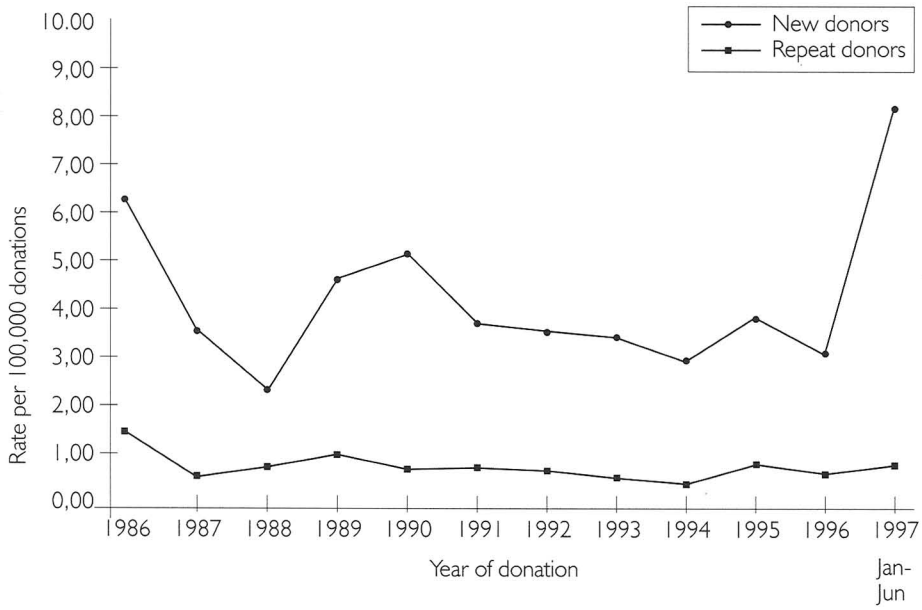
Several countries are now producing estimates of the residual risk from transfusion. An example of such an analysis from England is shown in table 1. For simplicity, the confidence intervals for the calculated risks are not shown, but they are generally relatively wide. In the figure, the risk from seroconverting donors is shown for HIV and HCV. In addition, risks due to false-negativity of assays (taking a probably conservative estimate of 98% sensitivity) and of risks due to process error are tabulated. An error rate of 0.5% has been used for the calculation, and again this is likely to be an overestimate in England as testing is fully automated, assays used employ sample and reagent colour monitors, and information transfer is fully computerised. Total residual risk is tabulated for repeat donors, and by extrapolation from seroprevalence data, for new donors. The situation for HBV is still under analysis. The risk from HBV seroconverting donors is similar to that for HCV. However, there is an additional element of risk from donors who may be at the žtail-end' of carriage (3) with subliminal levels of HbsAg but with persistent high titres of anti-HBc (due to chronic exposure to virus). In an analysis over several years at North London (unpublished data), only ¼ of investigated post-transfusion hepatitis B cases were due to seronegative donors in the window period. In the remaining ¾ of cases a donor with anti-HBc in the absence of HbsAg could be circumstantially implicated. At North London, at least, the residual risk from post-transfusion HBV is likely to be within the range of 1 in 50,000 to 1 in 200,000 $\pm$ appropriate confidence limits.

The English figures for risk can be compared with calculations from the USA (see table 2, courtesy of Dr. M. Contreras).

## Direct surveillance of post-transfusion infections

Central reporting, investigation and collation of transfusion-associated infections form the basis of the French žHaemovigilance' programme and the UK Serious Hazards of Transfusion (SHOT) scheme (4). These schemes provide direct evidence of the level of residual symptomatic (in most cases) risk of microbial infection from transfusion. Taken together with the calculated theoretical residual risks, a picture of the relevance of different microbial agents in an individual country, or in different countries, can be developed. If the prevalences and incidences of an agent (or agents) is considered to be comparatively high, specific additional testing interventions can be contemplated.

Figure 1 **a) HIV infected blood donations: UK**




Note: The higher rate of HIV in donations from new donors during Jan - Jun 1997 ic being investigated further.

**b) HIV infected blood donations: England and Wales**

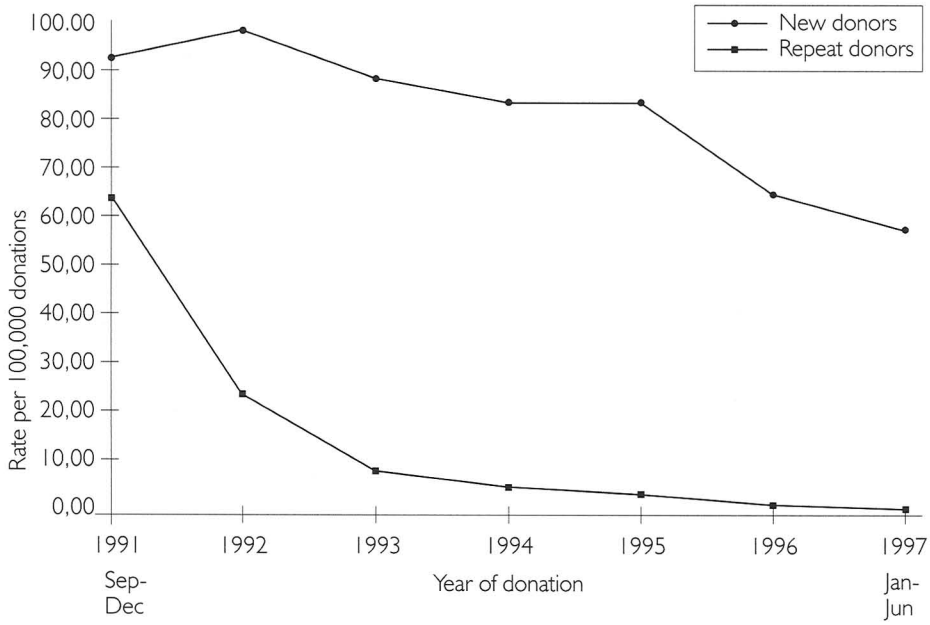


Table I.: Risk of infectius donation per 100,000 donations (England)

| | HIV | HCV | HBV |
|---|---|---|---|
| from serocon. donors | 0.015 | 0.059 | ?tailend |
| due to test intensitivity | 0.015 | 0.322 | carriers |
| due to process error | 0.004 | 0.079 | |
| Totals | 0.034 (1 in $3 \times 10^6$) | 0.460 (1 in $2 \times 10^5$) | |
| new donors | 0.319 (1 in $6 \times 10^5$) | 2.347 (1 in $4 \times 10^4$) | |
| repeat donors | 0.019 (1 in $5 \times 10^6$) | 0.204 (1 in $5 \times 10^5$) | |

*Soldan & Barbara, unpublished data*

Table II.: Estimated current risk of TTIS (Usa/Uk)
*Approximate estimated risk (per unit transfused)*

| Infection | USA | UK |
|---|---|---|
| Hepatitis B | 1 in 66,000 1 in 200,000 | 1 in 50,000 |
| Hepatitis C | 1 in 121,000 | 1 in 200,000 |
| HIV-1 | 1 in 563,000 1 in 825,000 | 1 in 2,500,000 |
| Bacterial contamination | | |
| • platelets | 1 in 2,400 1 in 15,000 | unknown |
| • red cells | 1 in 1,000,000 | unknown |

*Courtesy (M. Contreras)*

## Comparative microbial risks and additional testing

### HBV

In Spain, the percentage of HbsAg positive donations varies from 0.008 to 0.13% at different blood centres (table 3, courtesy of Dr. M. Carasa). The former rate is of the same order of magnitude as in the UK donor population overall. The 16-fold difference of HbsAg rate might stimulate consideration of additional safety measures to reduce residual risk, especially if post-transfusion infection surveillance reveals an increased risk in areas of increased HbsAg positivity rates in blood donors. Such measures may include the use of additional anti-HBc screening to offset risk from 'tall-end' carriers (3). Only high-titre anti-HBc results are indicative of donor infectivity and donors with concomitant anti-HBs (e.g. greater than 100 miμ/ml) would be immune and suitable as donors (5) if complying w3ith other donor qualifications. An assay to detect anti-HBc as sole HBV marker and high titre anti-HBs simultaneously is currently under investigation (6). Such an assay may be of unique value in a Mediterranean context, where the prevalence of 'tall-end' carriers may be significant.

### HIV

In the USA, despite the initial recommendations of the US Blood Product Advisory Committee (subsequently overturned by the Food and Drug Agency). HIV p24 antigen testing was introduced as an additional assay to reduce the risk of window

period transmissions. The projected rates of confirmed HIV-Ag positive, anti-HIV negative blood donors have turned out to be tenfold higher than the actual numbers detected. Only in areas of high acquisition rates of new infection, such as Thailand, is the introduction of HIV-antigen testing arguably cost effective.

Table III.: Blood donations infectious markers results Spain 1996
HbsAg

| BTS | Tested Units | Reactive U | Confirmed U | Percentage | Seroconvers. |
|---|---|---|---|---|---|
| 1 | 235,017 | 317 | 136 | 0.0578 | 9 |
| 2 | 34,309 | 59 | 17 | 0.0495 | 0 |
| 3 | 35,304 | 38 | 8 | 0.0226 | 3 |
| 4 | 30,566 | 11 | 11 | 0.0359 | 0 |
| 5 | 45,086 | 117 | 56 | 0.1242 | - |
| 6 | 22,728 | 15 | 4 | 0.0175 | 0 |
| 7 | 48,861 | 114 | 57 | 0.1166 | 5 |
| 8 | 78,128 | 106 | 30 | 0.0383 | 1 |
| 9 | 215,565 | 309 | 210 | 0.0974 | 9 |
| 10 | 29,526 | 88 | 39 | 0.1320 | - |
| 11 | 93,228 | 97 | 72 | 0.0772 | 2 |
| 12 | 194,246 | 409 | 206 | 0.1060 | 36 |
| 13 | 37,260 | 82 | 38 | 0.1019 | - |
| 14 | 25,353 | 43 | 2 | 0.0078 | 0 |
| 15 | 93,317 | 62 | 15 | 0.0160 | 0 |
| 16 | 10,837 | 5 | 5 | 0.0461 | 1 |
| 17 | 137,879 | 149 | 123 | 0.0892 | 0 |
| | 1,367,210 | 2,015 | 1,029 | 0.0752 | 66 |

*Courtesy M. Carasa*

## Emerging agents

*Human Herpes-Virus 8 (HHV8)*

HHV8 is the eighth human herpes virus to be described. It is white-cell associated and is the causative agent of Kaposi's sarcoma (7). So far it is only a theoretical risk to the safety of the blood supply but in countries such as Italy where relatively high rates of seropositivity (with wide ranges in rates across the country) have been reported (8), from 7.3% in North/Central areas to 24.6% in Southern parts, the possibility of (?selective) anti-HHV8 screening could be considered.

## Variant creutzfeldt - jakob disease (vCJD)

In the UK, where 23 cases of VCJD have been reported (4 of which were in individuals who had previously donated blood), a variety of measures have been put in place or will be considered following a formal Deaprtment of Health risk assessment (9). Obviously, the impact of differential epidemiology of potentially transfusion-transmissible agents is considerable.

## Conclusion

Any analysis of residual risk from existing or emerging agents of potential significance to transfusion safety has got to be based on detailed and extensive surveillance and epidemiological parameters. Only when carefully defined and painstakingly monitored data are available for analysis can sensible and cost-effective decisions be made for additional interventions such as extra serological tests. PCR (on single or pooled donations) and leucodepletion be contemplated.

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7. Blackbourn DJ, Ambroziak J, Lennett E, Adams M, Ramachandran B, Levy JA. Infectious human herpesvirus 8 in a healthy North American blood donor. Lancet 1997: 349; 609-611.

8. Whitby D, Luppi M, Barozzi P, Boshoff C, Weiss RA, Torelli G. Human herpesvirus 8 seroprevalence in blood donors and lymphoma patients from different regions of Italy. Journal of the National Cancer Institute 1998; 90: in press.

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# The urgent need of mutually compatible criteria and behaviour for blood safety in Europe

*Umberto Rossi*

(Department of Haematology and Transfusion Medicine, Hospital of Legnano, Milano, Italy; *ESTM President)*

It has become increasingly clear, in the last years, that the series of measures concerning blood donation and transfusion, taken by several governments in Western European countries, have been largely dictated by **fear** of transfusion-transmissible diseases (TTD) in the **general public**: this fear, transfused to **politicians**, has generated an **even deeper fear**, of possibly being criticised -and politically blamed- for not having done enough to protect the population from TTD [57, 62]. Both fears have been favoured by **lack of proper information** in the schools and universities, by the prevailing episodic or "scandalistic" attitude of large part of the media: that **receiving a blood transfusion is today by far one of the safest medical procedures in Western Europe**, would sound new and be hardly believable for many a European Union citizen! [12, 110, 137] Transfusion has been more often looked upon as a negative procedure, against which to defend our life, rather than a positive act under well established criteria.

The **"principle of precaution"** [12, 39, 48, 110], implying that no already available scientific evidence of danger should be necessary to justify preventive measures (legitimated unless scientific evidence of lack of danger should be available), has gained wide popularity in the world of decision-makers.

Two equally dangerous risks are facing Europe since some time: the "**overdramatization**" [110, 111] (in "developed") and the "**underestimation**" [42, 43] of transfusion risks (in "developing" countries).

We see how easy it is to increase expenditures for blood safety, and we are approaching in Western Europe the point, where **homologous transfusion could become one of the most expensive medical procedures** [62, 137] and absorb an incredible part of our public health economies.

Besides the risk of **transfusion-induced bankrupt** of our public health systems, many more are the **risks originated by "overdramatization"** [110]: the risks of ignorance, of social anxiety, of commercial slavery, of decisional mimicry, of bureaucratic regulatory strabism, of increasing political discrepancies from country to country, of international disharmonies in transfusion treatment, of decreasing voluntary donors and social solidarity, of emotional refusal of transfusion therapy by critically ill patient, of disaffection and disappearance of Transfusion Medicine specialists, to be regarded by now like an endangered species.

Efforts should be made to understand the **real dimensions of transfusion risks, as compared with all other possible risks**: not only viral transfusion risk, but all other risks involved in our profession; and the risks of life and death, of peace and war, of health and diseases, of joy and sorrow; and the risk of not being aware of risks, and not being able to properly face them [12].

On the other side, in "developing" countries, the "underestimation" of transfusion risks (often bound to a fatalistic political attitude and to a helpless professional behaviour) is at the origin of an even larger diffusion of TTD, leading sometimes to a further, unforgivable, risk: that **expensive technological investments could absorb the available financial resources**, in a well meant effort to "keep up" with richer countries: honestly believing this is the best and quickest way to reach the target of a nation-wide safe blood; but also leaving no money for **essential investments** in **promotion of voluntary blood donation**, in **education of donors**, in **information of the**

**public**, in **training of Transfusion Medicine specialists**, in **rational and economic organization of Blood Transfusion Services**, which are **far more important basic requirements** for building up a safe Transfusion System [23, 55, 65, 116, 118, 131, 151].

## Basic requirements for an acceptable safety of blood donation and Transfusion Medicine in Europe

It has been observed that legal and ethical issues, in our profession, are often perceived as **theoretical** and somehow **abstract** prescriptions, sometimes ignoring real problems and therefore difficult to be entirely observed, hardly answering to the needs of professional practice most of all in countries with limited resources.

Legal and ethical definitions are related to historical **periods** and to different **areas** of the world, and partly depend on **criteria** such as cultural background, traditional lifestyle, religious influences, political evolution.

To our aims, we need to specify their pertainance to an **historical** period (year 2000, beginning of the third millennium, 10 years after the fall of the Berlin wall) and to a **geographical** extension (our new broad Europe, as part of the world's global village).

**Law** and **ethics** may well be conceived as **complementary**, both aiming at regulating social and political life so as to ensure the respect of individual rights and the achievement of the highest social welfare [17, 120]. They exist in order to be applied, they must be applicable, and the measure of their value is also the degree of their **application**. They are at the origin of some cultural, social, political and professional criteria, leading to a series of **basic requirements**, all of them essential to build up an **acceptable safety of blood donation and Transfusion Medicine**, **today** and in the **future**, in all our **countries** and in the whole of **Europe** [120]:

1) A clear definition of what is meant by the medical **specialization in "Transfusion Medicine"** and the existence in the country of a sufficient number of dedicated **Transfusion Medicine specialists**.
2) The presence of a **minimum core of Transfusion Medicine competence** in the cultural background of general **doctors** and other specialists, of **nurses** and **technicians**.
3) A well functioning organization of **voluntary donation**, within the national system of public health and hospital assistance, with adequate consideration of **donors medical care**.
4) A general feeling of belonging to a **national**, but also to an **international (European) medical and transfusional community**.
5) A proper cultural approach to **blood safety** and **risk management**.
6) A widespread application of "**quality**" **principles**, in the frame of a quality management, to the national organisation (central and peripheral) of Transfusion Medicine.

I will try to analyse how these requirements have been fulfilled, so far, in Europe, thanks to the contributions of the **international** and **European Institutions** [17, 31, 32, 36, 47, 74, 150, 153, 154, 155, 157, 158], some **National Societies** [13, 88, 90, 113, 125, 127, 130, 141, 149], the **ISBT** (International Society of Blood Transfusion) [25, 53, 54, 126, 136, 149, 145] and the **ESTM** (European School of Transfusion Medicine) [95, 107, 114, 115, 122], firmly convinced that, for each of them, European harmonization is an absolute condition for an improvement of blood safety all over Europe.

## Definition of Transfusion Medicine as an autonomous speciality

Already at the first International Blood Transfusion Congress, held in Rome in September **1935**, the Congress President Professor Leone Lattes expressed the need for *"... discussions among researchers of different and multifold experiences, in a field that in some big countries has become* **a veritable medical speciality** *..."* [60].

After the brutal interruption of the second world war, during an "extraordinary session" of the third International Blood Congress in **Turin** in **1948**, at which SIBT was reconstituted, the Congress listed, among its *"accepted wishes"*, that "**in all countries should the theoretical and practical teaching of blood transfusion and of related subjects be organized**".

In June **1963** the **Council of Europe (CE)** issued some "**Recommendation on instruction in blood transfusion**" [29], followed in March **1985** by a **Recommendation including a "model curriculum for the training of specialists in blood transfusion**" [32]. The CE's recommendation was rather poorly implemented by member countries [125]. Neither the Directives issued in June **1975** by the **European Community (EC)** [28], concerning the reciprocal recognition of diplomas and certificates of specialist doctors, nor its amendments and addenda issued in the following years, ever included blood transfusion as a speciality.

The subject of specialist training had received some attention at the 1st **ISBT** Regional European Congress in **Lugano**, in **May 1989** [25], during a session on "**Training and education**". Further progress was made at the 1st SIITS-AICT Symposium for European Cooperation in **Cernobbio** (attended by representatives of 21 European countries), in **October 1990** [125], on "**Teaching of Transfusion Medicine**", aiming *"to verify and discuss the teaching of immunohaematology and transfusion therapy in Europe, starting with the training programme proposed in the 1984-1985 document of the Council of Europe"*. Its validity was accepted but the need for some reshaping of its contents was recognised. The recent European socio-political developments, leading to a broader-based Europe, were also taken into account.

More **problems** had emerged recently and had to be faced in the world of blood transfusion: prevention of blood-transmittable viral diseases, autologous transfusion, cryopreservation, therapeutic haemapheresis, bone marrow donation and transplantation, tissue banking, forensic haemogenetics, massive transfusions, information technology and data processing, etc. [84]. "**Blood Transfusion**" or "**Transfusion Medicine**"?, first of all. Was this choice just a matter of semantic preference, or maybe a fashion, or did it imply a more meaningful **definition** of the contents of our discipline and of its boundaries with other neighbouring medical disciplines [84, 125]?

As a result of these endeavours, a "**Proposal of a recommended minimum European curriculum of post-graduate teaching of Transfusion Medicine based upon the 1984-1985's Council of Europe's document**" [85], aimed at *"the development of nationally recognised training programmes which may -subsequently- find international recognition of their degrees and diplomas in Europe"* [32], has been discussed, amended and defined, by the European transfusional community, during the main session on "**Teaching and education in Transfusion Medicine**" [126] at the 3rd **ISBT** Regional (2nd European) Congress in **Prague**, on **15th October 1991**, with the critical participation of representatives of the Council of Europe and of the European Community; has received the **scientific consensus of the 1991 ISBT European Congress**; has been **proposed by the ISBT to the Council of Europe**, and has been **positively evaluated by its Committee of Experts** in Blood Transfusion and Immunohaematology in **May 1992**.

The **proposal** has been later proposed **to the European Community (EC)**, as a term of reference for evaluation of any future national curriculum, and for official recognition of "**Transfusion Medicine" as a "new" speciality**, reciprocally recognizable between member States, according to the 1975 EC Directives [28, 126]. The implementation of a "**free circulation" of Transfusion Medicine specialists** within the European Union would imply several possibilities of stages and work in other countries, with a very meaningful result of mutual professional training and a progressive levelling of national differences.

A bilingual (English and French) **training course on Blood Transfusion** (coordinated by Prof. W.G. Van Aken and Prof. B. Genetet [150]), started in 1994/95, in form of an interactive distance-learning course, handled by the CNED (National Centre for Distance Education), with a final examination by the Strasbourg University and the issue of a **diploma validated by the Council of Europe**. The course has been unfortunately discontinued, but this initiative could well be conceived as a "core" of a future unified **European diploma of specialisation in Transfusion Medicine** [3, 112].

## The Transfusion Medicine specialist

The core of the above proposal [84] lies in the following **definition of a Transfusion Medicine specialist**: *"the specialist in Transfusion Medicine is a medically qualified person, having a thorough knowledge and sound experience of* **clinical medicine** *and* **laboratory medicine**, *having achieved a specific training in* **general haematology, immunology** *and* **blood transfusion practice**, *who is capable to ensure a maximum of* **efficacy** *and* **safety** *-for the donor and for the recipient- for any procedure of blood transfusion, who is* **responsible** *for the* **planning** *and* **organisation** *of the collection, preparation, storage, distribution and optimal use of blood and blood products under a controlled scheme of* **quality assurance**, *who can assist and advise on any* **diagnostic and therapeutic problem** *of patients requiring transfusion, who is actively participating in* **research and development** *and who is able and willing to* **teach Transfusion Medicine further** *to doctors, medical students and any other collaborating professionals".*

In other words, the Transfusion Medicine specialist is the physician who provides the **bridge** linking the donor to the **patient** [126] and allowing the patient to be best helped by the donor.

## Transfusion Medicine teaching to undergraduate medical students

The **1963** Council of Europe's "**Recommendation on instruction in blood transfusion**" [29], it was recommended *"that each Government should consider including* **courses of instruction for medical students**".

While it was quite obvious that "the **national framework for the professional training**" of medical students should have been represented in every member country by the University system, alone or in conjunction with the **Blood Transfusion Service** national organization, it became increasingly evident that little attention was paid to the teaching of **undergraduate** medical students, suffering from wide European variations [84].

Also the interest of the **WHO's** "Global blood safety initiative" **(GBSI)** on the training needs in Transfusion Medicine [157, 158] was not specifically directed to the problems of **undergraduate** teaching.

The **marked differences in the organisation of medical teaching in member**

states, in fact, made it difficult to envisage a common frame in which the teaching of Transfusion Medicine to medical students could be given, at least before a certain European harmonisation of the post-graduate teaching for specialist formation could have been attained. The next logical step [81, 84, 135] did therefore appear to be the discussion of Transfusion Medicine teaching to undergraduate medical students [140], aiming at defining the desired level of necessary competence by medical doctors, during the 4th Regional European Congress of the ISBT in Barcelona, in 1993, leading to a "Proposal of a common minimum European curriculum for Transfusion Medicine teaching to undergraduate medical students" [135].

## The training of nurses and technicians in Transfusion Medicine

In the 1963 Council of Europe's "Recommendation on instruction in blood transfusion" [29], it was considered *"that... nurses... have to carry* heavy responsibilities related to blood transfusion practice*"*, and it was recommended *"that each Government should consider including* courses of instruction *for... b) nurses and midwives; c) laboratory technicians;* ...within the national framework for the professional training *of these categories of staff..."*.

Moreover, in the Council of Europe's Agreement on the training of nurses [30], signed in Strasbourg on 25/10/1967, it was clearly indicated that the theoretical and technical teaching should include "theory of blood transfusion" and the clinical training should concern "all aspects... of treatment by blood transfusion", including organisation of services and laboratory practice.

After the very limited number of observations obtained at the European meetings of Lugano (1989) [25] and Cernobbio (1990) [125], efforts were made in the ISBT European Congress of Prague (1991) [84, 126] to receive information on the training of nurses and technicians working in Transfusion Medicine in Europe; a report from a representative of the ICN (International College of Nurses) originated discussions as to whether, and how, subjects and programmes could be defined and included in a common integrated European proposal of training for nurses [92, 126]. In the meantime, some National Transfusion Medicine Societies had started organising satellite courses for nurses and technicians during their scientific Congresses, in the firm belief that they are an essential part of the team work in Transfusion Medicine.

This preliminary work of analysis, in the years from 1989 to 1993, suggested a further study of the problem, during a session of the ISBT European Congress of Venezia in 1995, leading to a "proposal of a recommended minimum European curriculum of teaching Transfusion Medicine for nurses" [134], based on a proper basic teaching during the 3 nursing school years, and the organisation and recognition of a specific competence, through a well designed system of accreditation certificates, for nurses having acquired experience in Transfusion Medicine.

## The situation of voluntary blood donation

Voluntary, non-remunerated blood donation is a precious heritage of pride for many European countries [82, 130]. The first Association (AVIS) was founded in Milan (Italy) in May 1927; the French Federation in 1949 (reorganized in 1972), several others followed. Independent blood donors Associations (or "Federations", or "Unions") exist nowadays in many European countries. In 1955 in Luxembourg the International Federation of Blood Donors Organizations (IFBDO-FIODS) was officially founded [130] by the Organisations of 7 European countries (Austria, Belgium, France, Great Britain, Italy, Luxembourg, Monaco); to date, the FIODS counts more than 80 members from the five continents.

All of us are aware of the importance of the **Federation of the Red Cross and Red Crescent Societies** (international), and of the national Red Cross Societies, in organising blood donors in **more than 10 European countries**. In some other European countries blood donors are not associated, or have been organised **around governmental institutions**.

And yet, in spite of all these organisational efforts, in some European countries blood donors are few and blood for transfusion and fractionation is insufficient [61, 82, 141].

At the Second SIITS-AICT Symposium for European Cooperation (**Cernobbio**, 6th October **1990**) on "**Voluntary blood donors Associations: present and future**" [125], attempts were made to compose a picture of European blood donation [82], and numbers of units of blood collected and of periodic (repeat) donors were estimated in 15 European countries.

**Differences** were observed [82] in the number of blood donors and in their motivations, in the ways of promotion of blood donation, in the organization of blood collection, in the public support to voluntary Associations, in the national legislations on the collection and distribution of blood, in the medical surveillance of blood donors, in the role of voluntary blood donors Associations in the prevention of diseases, in the relationship between donors and physicians; economic, social, political, ethnical, cultural, religious differences; differences between West and East, North and South. It became evident that a **European self-sufficiency in blood donation** could only be achieved as a result of **national and local self-sufficiencies** [82], and that many problems indeed are waiting for some solution by **political initiatives** of our National and European Authorities: intelligent legislation, even distribution of resources, international help, reciprocal integration, adequate blood collection, cost-effective plasma separation and fractionation. Proposals were also made of a European blood donors Association, of a European Community group of National Federations, and of a more active role and support to European developing countries by the Council of Europe and the European Community.

With the **fall of political walls** and the opening of borders between East and West, a new negative phenomenon has been registered in many Eastern countries: a worrying decrease in the number of voluntary blood donors and an obvious weakening of their motivations. As if the sudden lack of imposed discipline and material incentivations couldn't be substituted quickly enough by moral maturity and social solidarity. In a **survey of Blood Transfusion Services** of some **11 Central and Eastern European countries** (Estonia, Latvia, Lithuania, Poland, Czech and Slovak Republics, Hungary, Romania, Bulgaria, Albania and Slovenia), prepared by Prof. Heiniger [47] for the **Council of Europe** 1992-1993 co-ordinated research programme in blood transfusion, the **collection of whole blood donations** dropped in two years from 4.052.000 in 1989 to 3.426.000 in 1991, decreasing by 15,4%, in spite of a slight increase of 0,7% of the total population, resulting in a **decrease** of the number of donations/1.000 inhabitants of **16,0%**; decreases were as high as 17,6% in Poland, 23,0% in Romania and 36,6% in Bulgaria: giving evidence that **blood donation can't help being a reflection** of the political "health" of a country and of its national "cohesion".

As Prof. L. Hirszfeld already expressed in **1935** [50], in his opening address at the First International Congress of Blood Transfusion in **Rome**, "our science does not only express the intellectual progress, but also the **moral values of a nation**".

At the Fourth SIITS-AICT Symposium for European Cooperation (**Roma**, 6th June **1992**) on "**Mass-media and blood donation**" [127], the relevance of an intelligent and technically effective occupation of mass-media for the promotion of blood donation was adequately stressed. It was concluded that the **attention devoted by mass-media** to the necessity of increasing the number of voluntary non-remunerated blood donors is presently -all over Europe- still fairly low, and that a "**chronic**" **strategy**

**of attention** by mass-media -ensuring a stable and high level of promotional activity- is certainly far more productive and avoids any need for **expensive** "**acute**" **campaigns**, which seldom bring any positive results, but more often disconcert and disillusion [86].

In the two ESTM residential courses on "**Promotion and maintenance of voluntary, non-remunerated blood donation**" (in June **1996** [143] in **Santiago**, Spain, and in September **1999** [139, 142] in **Bucharest**, Romania), more than 100 participants from 14 European countries could exchange their experiences. Another ESTM course on the same subject is planned for 2002 in Lithuania.

A "**European Youth Forum**" on blood donation [116] has recently (September **2000**) taken place in **Italy**, organized by the **IFBDO/FIODS** and by the Italian **AVIS**, allowing more than 250 participants, from 13 European countries, to compare their different national situations, leading to a project of further cooperation to establish a network for the progress and harmonisation of voluntary blood donation in Europe.

## "Quality" donors

There is a general agreement that donors should be "**voluntary**" and "**non-remunerated**", always excluding "financial profit", according to the ISBT "**Code of ethics for blood donation and transfusion** [41, 53, 54]. The concession of free working time or of a "food coupon", for example, or of any other kind of material incentivation, is **not** compatible with the "**non-remuneration**" of the voluntary blood donation. A voluntary blood donor is somebody who has made a **free decision** out of a **personal conviction**, not resulting from any pressure of emotions or necessity, but originating from the **moral awareness** of the donation being a **social duty** from the healthy to the sick [80, 146].

A strong motivation is represented by the **feeling of social pride** given by the certainty of belonging to an undoubtely self-selected group of citizen. The **moral gratification** connected with this feeling is possibly the highest spiritual expression among the many motivations to blood donation, and is certainly the source of the active involvement of many donors themselves in the promotion of blood donation and in the active participation in campaigns of prevention against blood-transmissible diseases [21, 93, 116, 118]. Blood donors are therefore citizen endowed with particular feelings of **personal, social and moral responsibility**, giving their blood **voluntarily**, **freely**, **anonymously and periodically**: this is what we mean by "**quality**" **donor** [42, 131, 133].

The "critical" (if not sometimes dramatic) situation of **real** voluntary blood donation in many European countries is justifying to give a strong priority to its establishment, or reconstruction, as an absolute pre-requirement to any possible development of Transfusion Medicine [93, 99, 116, 118].

To this aim a powerful help is represented by a well organized **donors medical care** [116, 118, 130].

## Medical care of voluntary blood donors

Donor selection and care strictly implies an **organised medical control**.

If there is no doubt that a **strict medical control is necessary** (and will furthermore represent a powerful motivation for recruitment and retention of donors), a warning should also be given **against the** "**overmedicalization**" of blood donors medical control beyond the borders of its real necessity: **excessive proliferation** of laboratory tests may negatively impress the feeling of safety of donors, scare new prospective

donors, and reduce the number of active donors; **useless repetition** of physical examinations, radiographs and instrumental investigations, without adequate consideration of previously performed similar procedures (family physicians, work-place medical check-ups), may induce an unjustified increase of social costs of blood transfusion; **prevailing of more bureaucratic and legalistic worries** over sound medical acquisitions may lead to a scientific dequalification of Transfusion Medicine [49, 94, 101, 116].

The **highest degree of safety** will be given by **blood donors being fully aware** of their duties and made responsible for their decisions concerning blood donation [42, 80, 82, 118, 119, 133, 142, 143, 146].

A side problem in many European countries, where thalassaemia is widespread and blood donors are relatively few, is **the exclusion or the acceptance as blood donors of thalassaemia trait carriers**.

Although very few physiopathological and clinical data are available on the effect of blood donation in thalassaemia trait, **healthy thalassaemia trait carriers**, regularly enrolled as periodic donors, only very seldom show any sign of anaemia and should therefore in principle **not be excluded from blood donation**.

**Vaccination of voluntary periodic blood donors against hepatitis B virus** has been proposed in 1984 [124] as an **effective** and **economic** measure to drastically reduce the prevalence of post-transfusional B hepatitis, due to the decreased risk of donors being unnoticeably infectious at the time of blood donation. The availability of cheaper recombinant vaccines has made the proposal even more suggestive and practicable. The financial burden of the donors vaccination should not be considered an obstacle to its generalized extension: besides any medical or moral considerations, the cost of reagents for repeated markers investigations, which could obviously be spared, accounts for much more than the actual cost of vaccination [40, 83, 97, 104, 105, 121].
The **promotional impact on donors recruitment**, arising from the appreciation of a concrete benefit being offered to voluntary donors, is an other important side-effect of the vaccination campaign [116, 124, 138].

It is mandatory that donors with markers of blood-transmissible viral infections, or other abnormal laboratory or clinical findings, should be **notified** of their situation by the Blood Transfusion Centre physicians under the strictest medical **confidentiality**, and enrolled in a **regular follow-up in donor care clinics**, either by the Transfusion Centre itself, or in close collaboration with other specialist out-patient Departments [16, 116, 118, 119]. Medical care of blood donors is a price that the community has to pay, being justified not only by **ethical considerations**, but by its **positive effects** on blood donors recruitment and retention as well.

If all procedures relating to motivations, promotion, recruitment, retention, organization and medical care of donors are properly conceived and performed, many blood donors indeed will become **highly committed partners of the Blood Transfusion Service** [82, 93, 106, 130].

## Education to voluntary blood donation during military service

The **number of voluntary blood donors** in Europe is subject to **wide variations** [82, 93, 119] in different countries (irrespective of their affiliation to European Union, or Council of Europe, or "geographical" Europe), and is often **inadequate** to the growth and selective needs of modern medicine, mostly in Southern European countries.

**Compulsory military service (CMS)** is still present in many European countries (mainly South-European), conceived as a civic duty, involving a considerable part of the male population [89, 104, 105]. **Alternative civilian service (ACS)** is offered in some countries

to individuals unwilling to engage in CMS. The peculiar features (both technological and characterial) of modern war have made military Defense a specialised job and led many countries to build up an army mainly -or only- based on **professional military service (PMS)**. While on one side CMS has become **obsolete** from a **military** point of view, on the other side -being mostly conceived as purely military- CMS is also **failing** to make the best use of its precious opportunities for **civilian** education and training to professional abilities, civic behaviour and community feelings: not to speak of ACS, often reduced to useless and bureaucratic clerical tasks.

It may then be high time for a collective European meditation on the convenience of **abolishing CMS and ACS** and **reinforcing PMS**, whilst instituting for **all** citizen, in **all** countries, a really **compulsory military-civilian service (CMCS)** (under a combined responsibility of the Ministry of Defence, Education and others), whose main aims should be [104, 105]:

1) **Integration and back-up of professional Army** in war and catastrophes.
2) **Education of character** to social solidarity, ethnical tolerance, sexual responsi bility, civic behaviour, community feelings.
3) **Professional and technical training**, complementing previous scholastic teaching
4) Employment in **initiatives of social utility** (public works, agriculture, forests, environment, medical and psychological assistance, etc.).
5) **Education to medical responsibility, blood donation and Transfusion Medicine**.

This last goal is **already receiving attention in some countries, during CMS**, at present time. CMS is indeed long enough to allow an effective deep **education to blood donation**, through lectures by Transfusion Medicine specialists, group visits to civilian Blood Transfusion Centres, joint activities with groups of periodic voluntary blood donors, thus acquiring knowledge of the nature of blood and blood products, and being initiated to **proper blood donation** [104]. Through repetition of blood donation, the attitude to periodical blood donation can be consolidated during the whole period of CMS (or future CMCS).

"**Military-initiated**" **donors** would be likely to remain periodic blood donors in later civilian life, so greatly contributing to reinforce feelings of appreciation of the CMS (or future CMCS) by the general public.

**Vaccination against HBV** would greatly increase the quality and safety of blood donated by military (or future military-civilian) donors. Increased awareness can be reached of many problems concerning blood **safety** (prevention of hepatitis and AIDS, sexual education) and medical **aptitude** to blood donation (genetic counselling for red cell hereditary traits as thalassaemia, Hbs and G6PD), so exerting a further positive side-effect on public health.

Positive **experiences** on the above issues have so far been accomplished in Italy, Portugal and Spain [138], and in other European countries. Noteworthy the experience of Croatia, where blood donation was necessarily intensified during the war period, resulting also subsequently (in peace time) in a higher percentage of blood donors in the general population [104, 105].

The present **consistency of military blood donations** in Europe, however, although not negligible, is far from being optimal. The presence sometimes of some relevant fringe-benefits (licence, days-off, food supplement, etc), moreover, casts some shadows on its really "voluntary" nature. **Blood donation by military citizen** should be made as similar as possible to the one by civilians: same Centre, same procedures, same times, same organization, so that by itself could allow reciprocal acquaintance and would become an important element of integration. Ultimately, every military setting (barrack, headquarters, school, centre, etc) should be "**twinned**" with a

particular Blood Transfusion Centre, and a **common** annual programme of activity should be laid down and accomplished.

In the past 6 years, increasing interest for the promotion of voluntary blood donation has been shown during the last 3 **NATO Blood Conferences** (Istanbul, **1994** [89], The Hague, **1996** [138], Lisbon, **1998** [104, 128, 129]).

**Inquiries** on the **involvement of military service in the promotion of voluntary blood donation**, and on the **planning of military-civilian co-operation in emergency Transfusion Medicine**, have been proposed at the last 5th NATO Blood Conference in **Lisboa** in **1998** [104], and a preliminary report has been given at the last Conference in **Washington**, in November **2000**.

## Belonging to a European blood donation and Transfusion Medicine community

The initiatives taken in the **last ten years**, in the whole of **Europe**, by the ISBT, by some National Scientific Societies and by the ESTM have considerably helped to clarify the theory and practice of Transfusion Medicine in most European countries and to establish some **network** of scientific and professional communication, to the benefit also of countries of other continents (Africa and Asia) bordering the Mediterranean Sea.

The **birth (in April 1992)** and the rapid **growth** of the **European School of Transfusion Medicine (ESTM)** are a clear witness of the profound need for increasing harmonisation of the teaching of Transfusion Medicine **within a geographical Europe wider than the "political" definitions**, given by the European Union and the Council of Europe.

The **ESTM** is a non-profit Association under the Italian law, managed by a Council of Administration and an Executive Committee, and guided by European Scientific and Advisory Committees.

The **aims** of the ESTM were defined as to provide a specialist teaching of Transfusion Medicine, of an international and European character, for specialist doctors already established from a scientific and professional standpoint, physicians, other graduates and para-medical personnel under specialist training [95, 99, 107].

The establishment of the ESTM has been the result of a series of study documents and discussions on the teaching of Transfusion Medicine, originated by the **Council of Europe** (in 1963 and 1985) [29, 32] and developed by the **ISBT** [25, 126, 134, 136, 140] within its European Regional Congresses and by the Italian Society of Transfusion Medicine **(SIMTI)** [90, 125, 127, 130, 141] through its "Symposia for European Cooperation" (from 1990 to 1994), following the recommendation issued, in 1989, at the end of the ISBT 1st European Regional Congress in Lugano [25].

- **Teaching of Transfusion Medicine** *(U. Rossi, J.D. Cash: editors [125])*

  *Proceedings of the First SIITS-AICT Symposium for European Cooperation - Cernobbio (Italy), 1st October 1990*

- **Voluntary blood donors Associations: present and future** *(U. Rossi, V. Fresia, B. Genetet: editors [130])*

  *Proceedings of the Second SIITS-AICT Symposium for European Cooperation - Cernobbio (Italy), 6th October 1990*

- **Teaching and education in Transfusion Medicine** *(U. Rossi, J.D. Cash: editors [126])*

  Proceedings of the main session of the 3rd ISBT Regional (2nd European) Congress - Prague (Czechia), 15th October 1991

- **Therapy with plasma and albumin: production and clinical use** *(U. Rossi, W.G. Van Aken, M. Orlando: editors [141])*

*Proceedings of the Third SIITS-AICT Symposium for European Cooperation - Rome (Italy), 6th June 1992*

- **Mass media and blood donation** *(U. Rossi, I. Cipriani, V. Fresia: editors [127])*.
  *Proceedings of the Fourth SIITS-AICT Symposium for European Cooperation - Rome (Italy), 6th June 1992*
- **Teaching of Transfusion Medicine to undergraduate medical students** *(U. Rossi, H. Seyfried: editors [140])*
  *Proceedings of the Symposium of the 4th ISBT Regional (3rd European) Congress - Barcelona (Spain), 15th June 1993*
- **Therapeutic haemapheresis** *(U. Rossi, A. Bussel, M. Valbonesi: editors [90])*
  *Proceedings of the Satellite Symposium for European Cooperation - Genova (Italy), 9th June 1995*

Common features of these **European Symposia** have been the **recognition** of the present situation possibly in all countries of the new "broader" Europe, the **trial of "transfusing"** all the scientific data and documentation work gathered by the Council of Europe and by National Societies into the European Community, and the elaboration of some concrete **proposals** and **guidelines** for further harmonisation within Europe.

**51 courses** have so far been organised in **21 European countries** (Russia, Spain, Italy, Greece, Switzerland, Norway, France, Belgium, Czechia, The Netherlands, Portugal, Great Britain, Slovenia, Germany, Austria, Croatia, Estonia, Poland, Israel, Romania and Slovakia). More than **80 coordinators** and more than **380 teachers** have been involved, from **23 European countries** (and some from Australia, Brazil and USA). **Participants** have been so far **more than 2.000**, from **35 European countries** (and some from Canada, Argentina, Cuba, Brazil, Hong-Kong, Egypt and Gambia). A course, in January 1999, has been co-organized in Senegal [95, 99, 107, 115].

In the last ten years, opportunities have been given by some National Societies (Czechia, Germany, Israel, Italy, Portugal, Switzerland, Turkey) during their Congresses to discuss **European issues** concerning education in Transfusion Medicine. Many National Societies, or equivalent Institutions (Croatia, Czechia, Estonia, France, Germany, Greece, Israel, Italy, Norway, Poland, Portugal, Romania, Slovakia, Slovenia, Spain, Switzerland), have been actively collaborating in the **preparation of ESTM residential courses** [95, 115, 119], some of them more than once (Czechia, Greece, Italy, Slovenia, Spain). A concrete financial **support**, through the sponsorization of participants's fees, has been given to the ESTM residential courses occasionally by the British, German and Polish Societies, and periodically by the Italian Society. ESTM courses have been increasingly taking place in **Eastern European countries**, touching so far Russia, Estonia [14], Poland, Czechia, Slovenia [20], Croatia [27], Romania [139, 142], and Slovakia [59].

The Royal College of Pathologists (London), in 1995, has recognised ESTM courses as being appropriate for **Continuing Medical Education (CME)** purposes, enabling course attendants to receive CME credits at the rate of one credit per hour [107, 109, 119]. The recognition has been awarded again in 2000. An "**ESTM Fellowship Programme**" has been established, to collect funds in order to enable Eastern European Colleagues to participate in ESTM courses. A **study group** on the teaching of Transfusion Medicine to undergraduate medical students has been constituted after the ISBT European Congress of Barcelona in 1993. Prospects and achievements of **Transfusion Medicine teaching** have been discussed in scientific Congresses of **National Societies** in Czechia (1993, 1994 and 1998), Israel [122] (1993), Germany [88] (1993), Turkey [117] (1993 and 2000), Spain (1994), Portugal (1994), Italy (1996), Slovakia [59] (1997), Macedonia [118] (2000), Ukraine [120] (2000) and of the **ISBT** (Taipei [107], 1999; Vienna [115], 2000).

A **translation of the AABB Technical Manual into Russian** will soon be ready, to be sponsored by Institutions and Firms and distributed free to doctors and technicians

working in blood transfusion in Russian-speaking countries. A **"twinning programme" between Romanian and Italian Blood Transfusion Centres** has started in 1998, in agreement with the WHO and the Romanian Government, and is currently developing thanks to the help of many Italian Colleagues. The participation to some ESTM courses of a few Colleagues from South America has brought the idea that an educational initiative similar to the ESTM could be incubated, and proposed, in **Latin America**. This possibility has been discussed during the **ESTM "Iberic" courses** (in Spanish and Portuguese), successfully performed in 1996 and 1998, and will be further discussed in the next "Iberic" course in 2001.

To ensure a wider diffusion of their contents, it has been decided that ESTM course Proceedings will be published -in updated editions- as **books**, on sale at a cost price, and shall be soon available at an **Internet** site. The proposal of a distance-learning pluriennal specialization course, leading to a **European specialist diploma of Transfusion Medicine**, has been discussed and approved by the ESTM Scientific Committee, and is waiting to find the way to overcome the many obstacles to its implementation.

The ESTM courses have been performed, at varying degrees of complexity, dealing with **many aspects of** Transfusion Medicine, including promotion of voluntary blood donation [139, 142, 143], detection and prevention of transfusion-transmissible infections [10, 14], blood safety and transfusion risks [12], emergency Transfusion Medicine, autotransfusion [20, 108], haemapheresis, quality assurance and quality management [27, 35], immunohaematology, clinical use of blood [109], prospects of Transfusion Medicine [63].

Some **relevant national differences** still exist in different countries or areas of Europe, waiting for proper recognitions, studies and solutions.

**Issues and problems** such as the organization of real voluntary non-remunerated blood donation, the consistence of periodic donor population, the optimal index of donation, the contribution of autotransfusion, the development of bloodless surgery, the organization and responsibility of Blood Transfusion Services and plasma fractionation plants, the economic conditions of the supply of plasma related to the need of plasma fractions, the definition of the real clinical need of albumin, the extent of genome testing, the implementation of leucodepletion, are all of paramount importance for the future of Transfusion Medicine in Europe.

## Blood safety

**"Safety"** has a probabilistic nature. We can **"increase" safety** by understanding, counteracting and **"reducing" risks**. **Absolute blood safety**, and "zero-risk", do not exist [1, 10, 12, 57, 99, 110]. But **"maximum" blood safety** could be reached. How? Not with blood testing **alone**. Blood safety is a multifactorial human achievement and can only be **built** gradually, by steps, of which blood testing is of course an extremely important, but not the only one [33, 37, 96, 131, 133]. **Blood testing** must always "come **with**" a series of measures and behaviours aiming at transfusion safety [12, 36, 49, 94].

What should, then, "come **first**"? Our answer is: **"education of people to quality"** [44, 101, 116, 118, 131, 133]. Donors, medical doctors, transfusion specialists, health professionals, hospital administrators, public health officers, politicians, journalists, teachers, priests of good quality: **all** of them are really necessary to build up blood safety [101 116, 118]. Blood safety, however, is mostly the result of good blood donors and physicians: responsible blood donors, and knowledgeable physicians, caring about a good quality of clinical indications [101, 103, 109, 118].

## Quality of medical doctors and of clinical indications

General practitioners, hospital doctors, Transfusion Medicine specialists: **all** are important for an acceptable blood safety and for a good quality of clinical indications. The "**quality**" **of clinical indications** to transfusion [34, 101, 103, 118], however, mainly coincides with the "**quality**" **of the prescribing clinician**, which in turn depends on the **quality of his medical curriculum**. It is essential that the **medical undergraduate curriculum** [118, 135] implies information and "education" concerning blood donation and blood transfusion, enabling him to become aware of clinical indications of transfusion in his medical practice.

The "**quality**" **of clinical indications** is obviously the result of them having been weighed against all possible **side-effects**, or real **contra-indications** (as, for example, circulatory overload in patients with congestive heart disease), and of the **intrinsic risks of transfusion** having been adequately considered [132].

Silly sentences such as *"the best transfusion is the one never given"*, on the other side, may run the risk to become dangerously popular, as a reaction to an indiscriminate and unnecessary use of transfusion. *The* **best transfusion** *is the one given when it is really* **necessary**, *on proper clinical* **indications**, *being conscious and after careful evaluation of its* **side-effects**, *performed with a selected blood* **component**, *and adequately expecting and evaluating its* **beneficial effects** [123, 132].

A definite progress in blood safety, and in the quality of clinical indications, is to be expected by the implementation of Hospital Transfusion Committees [65] and of local, regional and national schemes of haemovigilance [19, 73, 91, 98, 100, 102].

## Increasing blood safety by education and quality management

The **basic concepts inspiring quality management** [15, 35, 117], that are usually understood, possessed and practised by anyone making part of any quality system, can be described as follows:

- general feeling that the results of the system (products, service, etc.) depend on **all** members of the system;
- distribution of jobs and tasks according to the individual role and abilities of **each** member of the system;
- clear **definition of roles** among persons and groups within the system, integrated in a **general frame**;
- awareness of a **personal responsibility** by any member of the system, not conflicting with the acceptance of a variety of different levels of responsibility, and of a higher responsibility for its **coordination**;
- **common desire of improvement** of the efficiency, efficacy and public image of the system;
- understanding of the advantages of **written documentation** of all steps of the personal and common work;
- feeling of initial adequacy, but of the need of personal **continuous improvement** as well, by **every** member of the system;
- awareness of the need of a programmed specific training to **increase personal abilities**, to the general benefit of the system;
- involvement of **all** members of the system to look for and find out "**non-conformities**", to report them, to correct and prevent them;

- increase of **mutual knowledge** between members of the system, improvement of personal relationships, easier acceptance of a shared discipline;
- improvement of the **relationships with "customers"** (donors, patients, colleagues) and of their appreciation and respect towards the system;
- gratification from being recognised -whatever the level of competence and responsibility- as "**essentia**l" to the system;
- feeling of personal satisfaction, and of humble pride, to **belong** to a "quality" system.

How do these basic "quality management" concepts coincide with the **concepts presently applied to everyday's work in Blood Transfusion Services** all over Europe, and to its wide variety of models of organization and performance? Can **education to "quality management"**, being fairly independent from financial resources and rather addressed to human behaviour, be considered an **adequate common tool to progress towards decreasing national differences concerning blood safety?**

It may be useful, and encouraging, to analyse the **similarities** between **"quality concepts"** and **existing "working concepts"**:

A) **Most of the "quality concepts" are already present**, felt and practised in the organisation of Blood Transfusion Services.

Quality control in laboratory work and in preparation of blood components, double-check controls in procedures of acceptance of requests and release of results or units, need and acceptance of written documentation in all fundamental steps of blood from the donor to the patient, validation of test results and of units delivery, clear perception of transfusion activities as a team work, frequent consultations of co-workers in common meetings, deep acceptance of the need of continuous education for all the personnel, acquaintance with written rules and service orders for the most delicate sectors of our work: all these are but a few most essential aspects of our already existing behavioural predisposition to be permeated by "quality concepts".

B) Accordingly, **also the main forms of teaching, learning and training** practised in Transfusion Medicine seem to adequately correspond to the learning requirements imposed by quality systems.

Although widely different in their external organizational shape, all Blood Transfusion Services already largely practise -in order to keep and improve their present standards of competences and performances- the following "didactic" behaviours: continuous and self-perpetuating teaching "in the field"; learning to teach by teaching; desire to learn requiring a basic belief (that we don't know enough) and a moral decision (that we want to know more); learning by reading and studying; learning by hearing and by talking and discussing; learning by writing (synthetizing, schematising, reporting); learning by working, meaning both by watching and by doing; learning by watching other people doing the things one wants to learn; learning by doing things, being watched by other people.

C) **Most of the motivations implied for a good learning of quality criteria** are already present in most of the personnel of our Services, and are well expressed by the very meaning of the word **"watching"**: which is beyond seeing, looking, noticing; it implies an intellectual trend to perfection, a social desire of interaction, a moral urge to share, a personal feeling of interest and solidarity.

D) The present explosion of "quality" criteria, meetings, rules, proposals, regula-tions, initiatives, courses, fashions, impositions, interests, temptations may be con-fusing for most of us, and maybe wrongly lead us to the dreadful conclusion that "quality",

for us, could only start "**after**": *after* money has been poured in, *after* automatic equipment has become available, etc. But if we are "watching" these phenomena carefully, with the same degree of attention and involvement we are used to, we may easily learn that **we only need to "increase" quality**, analysing identities and "non-conformities" with all what we presently do, and to quickly adjust our organisation to the standard requirements of a quality system.

E) The **rules of "quality"**, apparently so invariable and standardised, remind me of the psychological difficulties most of us experienced when computers stepped in our organisation: they looked to some of us as limiting our freedom and exacting our brain to adjust to their schemes, but we quickly learned to discover how intelligent we were in accepting them.

F) I feel that any psychological resistance to accept the **heavy workload of introducing a quality system** in our long-established work organisation could be easily overcome by considering the very high financial costs, moral unsatisfaction, and professional risks of **"non-quality"**.

G) **Learning to teach "non-quality", and teaching to analyse and avoid its (so far little recognised) disastrous disadvantages**, may well turn out to be the most important didactic task for all of us in the next future.

**"Quality as a way of life"**, once generally accepted and practiced, can greatly contribute to quickly reduce throughout Europe the existing huge differences in Transfusion Medicine performance and in blood safety.

## A proper cultural approach to transfusion risk management

A recent ESTM course (Bruxelles, 26-29 February 2000), on **"Risk perception and risk assessment in transfusion practice: how to achieve a sound transfusion practice based on scientific truth"** [12], has initiated a wider discussion on the current criteria of scientific, professional and political behaviour concerning the **residual** transfusion risk in Europe [11, 57, 58, 144, 148].

The aim of the course was to give the participants a sound knowledge on the probabilistic nature of risk and of the **real dimensions** of risks in today's life [75, 76, 147, 152], from the existential, natural, environmental, behavioural, economical risks to the biological and medical risks in general [2, 18, 69, 77], more specifically focusing on the risks (not only viral!) of transfusion practice [4, 5, 7, 38, 70, 159, 160]. To obtain that knowledge of its medical advantages and clinical indications could be weighed against its risks, **scientifically** and **comparatively evaluated** [75, 76, 77]. The ultimate aims was to make European transfusion specialists more aware of their responsibilities in exerting a positive influence on mass media, on public opinion, on administrators and on politicians in order to make a **correct use of public resources**, based upon **scientific evidence** of the usefulness of their allocation and upon a **critical analysis** of cost/benefit ratios, influenced not by fear but by reason [1, 71, 148].

**Haemovigilance surveys**, in "developed" countries, have shown how important by now, as compared with viral risk, have become some **other** transfusion risks, like bacterial contamination [6, 9, 72, 159], wrong identification [66, 67, 68, 137], and improper clinical indications [5, 103].

Public opinion should be encouraged to a **better perception** of the real dimension of life risks in general, and of medical risks in particular [45, 52, 58, 64, 78, 79, 147], so that **decision on possible further reductions of transfusion viral risk** could be correctly understood, evaluated and discussed by all citizens, and maybe submitted (in some cases) to their own decision.

This **critical re-evaluation of the existing measures on blood safety** (further developed in the recent ISBT Congress in Vienna) should not loose awareness of the **widely different situations existing in today's Europe**, where a generalized blood safety hasn't yet been reached [111, 118, 120, 156].

## The future of blood safety, a challenge for the whole Europe

The time has come for a **more responsible collective meditation** on the present strategies of prevention of the relevant transfusion risks [3, 8, 22, 24], and on the **drafting of national and European regulations concerning blood safety**.

We are, indeed, facing the **risk that an uncontrolled progress in the practice of Transfusion Medicine could lead us to a situation**, where **differences in the quality of transfusion treatment between European regions and nations** could increase, rather than diminish, due to a different pace, and most of all to a different concept, of progress [74, 110, 111, 116, 118]. Measures should then be taken (at a political, scientific and professional level) to ensure that "developing" countries could **develop faster** [111, 116, 119], to reduce the quality gap as soon as possible.

**The "door" of blood safety should first be fully open, all over Europe** [43, 44, 131, 133], at the lowest possible financial cost, counting mostly on the **education of people** (at all possible levels) and on the generalized application of **simple screening procedures**: the **basis** (and quickly!) **before the top** of the pyramid!

More sophisticated (and expensive) technologies can **only** have a significance if they are implemented **to integrate and perfection already existing means**, never to substitute and bypass them.

To this aim, to counteract the **risk of an increasingly diverging quality** of Transfusion Medicine in Europe, money is far less important than **education** and **political awareness** [46, 51, 110, 111, 116, 118]: no decision on blood safety in the West should any more be taken without a clear insight into its reflexes on the blood safety of the whole of Europe, that must become a priority interest for all European Nations.

Prof. Cazal's introduction [26] to a Council of Europe's document [31], in 1983: *"to create a "Red Europe" ... and to assure "***Homo Europaeus***" of the same security as regards transfusion -the same transfusion rights and duties- wherever he lived and travelled")* can be appropriately quoted as an obvious motivation for the **harmonisation of blood transfusion practice**: that should be a matter of common and equal concern, in all European countries, for the Ministries of Health, Education and Defence, which should be jointly responsible of a governmental, internationally linked, **programme of blood donation and Transfusion Medicine** [104, 119, 120].

Let us consider this as one of our challenges for the third millennium of our history.

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# Blood safety in European countries with limited resources

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During the last decades, attention focused more and more on blood transfusion and a safer blood product. Policies turned to generally accepted standards and recommendations, for increasing blood safety, at international level, with national reflection. In this respect, the World Health Day theme of the year 2000 was blood safety, with the well-known logo: "Safe blood starts with me", underlining the key role of the average individual in the safe blood reserve and supply.

European countries with limited resources had to adjust quickly to the continuously changing scientific panorama, but also to the local political, economical and therefore social changes that occurred in the same period. If one would have to compare the present situation, to what was existing 10 years ago, the effort and results that have been obtained are remarkable.

At the beginning of the 90s, Blood Transfusion centers where generally hospital based, with very few exceptions, where such institutions were existing on their own. The National Blood Transfusion Service was a conglomerate of many small centers, with governmental budgeting and a very low cost-effectiveness. There was no legal frame for the system to function, nor a National Program developed locally. Blood donation was generally paid, a few volunteer non-remunerated donors being registered although, but mainly for family donations. The higher number of blood donors was due to the political side of the act, being considered in some ways an ideological obligation (generally managed through the National Red Cross).

Blood was collected into glass bottles, the recipients being sterilized and reused many times, while testing was incomplete, performed with locally produced reagents, not complying even to basic quality requirements, as considered today.

Whole blood was used in general, only 20 to 40% blood units were processed into labile blood components, as red cell concentrate (sometimes washed), cryoprecipitate and plasma. Separation techniques where performed in completely open circuit, with low level of standardization or GMPs. Outdated plasma used for fractionation in local existing facilities, was the source for albumin, IM immunoglobulin and anti-D specific globulin, lyophilized plasma, as well as the production of blood grouping reagents, dried thrombin etc. A constant shortage of coagulation factors had to be considered, the only treatment available for haemophiliacs was cryoprecipitate or fresh frozen plasma.

The heterogeneous development of countries in Central and Eastern Europe during the last 10 years was reflected also on their National Blood Transfusion Services. Increasing differences appeared after 1990, linked to the social, economical and political problems of the area, wars and natural calamities, the new countries emerging out of unions and the sudden opening to information and setting up of own standards and priorities considered.

Efforts started to concentrate on blood safety, with national authorities commitment, so that now, a legal frame is present in almost all European countries (or seriously taken into consideration) ensuring the regulatory basis for the National Blood Transfusion Service to function. It is interesting to note that in most of the cases where legislation on blood collection and use exists, systems are generally organized on a centralized basis, with potential options, more or less open to local strategies.

Blood donation is apparently non-remunerated in many countries of the area, with a legal biological compensation in food and days off for the gift of blood. In the few cases where blood donation is still paid, an issue for voluntary blood donation, at least using a transient phase as previously specified, is considered. Some benevolent blood donors associations have already been constituted, with an increasing role to play in this action.

Blood collection was switched to plastic bags. Nevertheless, there are still places, where due to a major limitation of resources and supplies, sterilized glass bottles are also used. Fortunately, these cases are rare and related to limited areas. Testing is generally performed in conformity with international recommendations, for ABO blood grouping and transmissible disease, using standard kits.

The fractionation index of whole blood turned to more than 80% in certain areas, increasing the use of labile blood components. Naturally, for a clear outcome, the percentage of labile blood products has to be related to the general blood collection figure. Several types of labile blood products are available, including pediatric units in most of the countries of the area.

Plasma for industrial use is fractionated either locally (merged fractionation -plants), or outside the country based upon contractual agreements. The storage capacities for frozen industrial plasma are still a problem for many Blood Transfusion Services in the region.

It is important to underline the fundamental changes in structure and strategy have been initiated, backed up by international support programs (EC, CE, WB, WHO), for increasing blood safety and availability.

Major progress has been achieved, but many problems are still unsolved. And generally speaking, we face many common problems, such as:

- self sufficiency by limitation of needs,
- constant decrease of voluntary blood donors,
- need for plasma fractionation facilities/ issues,
- accurate haemovigilance feed-back,
- cost efficiency of introducing high cost-procedures, such as leukodepletion, NAT testing.

Due to the high sensitivity and high cost of the whole transfusion medicine chain, it is of major importance to have stable decision-making mechanisms and properly informed decision-makers. Setting up the example of scientific evidence based decisions will avoid wrong allocation of already limited funds and will enable a reassessment of priorities to be followed.

Extensive pro-donation campaigns are needed for public information and education, with media support. Altogether with continuous training programs for the BTS staff (to comply and constantly update quality requirements), as well as guidelines and specific training for clinicians in transfusion medicine will enable a new understanding, at different levels, of the cost-benefit challenge in terms of blood safety.

# Transfusion Risk and its perception in a wider context

*Virge James, Kate Soldan, John Barbara*

## Introduction

In 1818 James Blundell carried out the first blood transfusions between humans . Over a 10 year period he transfused 11 patients, 5 of whom died.

Since then transfusion therapy has developed and is now one of the cornerstones of modern medical practice. The biology of transfusion has come under intense scientific scrutiny and continues to develop .These scientific developments form the sound basis of safer blood transfusion A new perspective however has opened up in the past few years: the risks of transfusions, the assessment of such risks and the role of public perception of these risks for the future development of transfusion therapy.

An ESTM course in February 2000 in Brussels entitled " Risk Perception and risk assessment in Transfusion medicine: how to achieve a sound scientific practice based on scientific truth " (Ref 1) explored this topic in some depth . It became clear that communicating the risk of transfusion to the public and recipients and potential recipients of blood components and products is a complex issue and collaboration with disciplines outwith medicine is essential. Much work has been carried out in the social sciences in the field of communication, understanding and behaviour which the transfusion services of today would benefit from studying and applying.

This paper will focus on :

1. Current "professional" knowledge (transfusion medicine specialists) of the risks of blood transfusion.
2. Attempts to convey the "professional" knowledge to other professionals and lay public without distortion .
3. The options for risk reduction
4. The cost/benefit debate in transfusion therapy

## Current professional knowledge of risks

Knowledge of the risk of transfusion has been obtained, and continues to be learnt, from several different approaches - each with limitations. Perhaps the most informative are:

1. Follow-up of recipients of blood transfusion for any signs of complications.
2. Surveillance of the complications of blood transfusions.
3. Case histories.
4. Estimation of the number of expected complications based on modelling the variables that give rise to complications.

Follow-up of recipients has become an unproductive approach as the risks of transfusion have fallen. A recent study of the recipients of over 21,000 blood transfusions in England found no HIV, HBV, HCV or HTLV infections (Ref 2). Another disadvantage of this approach is that results are out of date as soon as transfusion practices change.

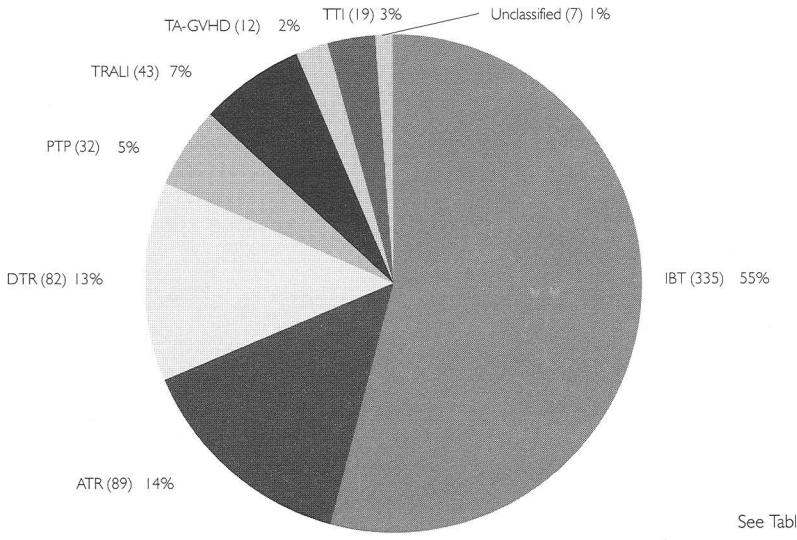
Many countries now have a system for monitoring complications of transfusion. In the UK we have a surveillance system called the Serious Hazards of Transfusion (SHOT) (Ref 3). Six-hundred and nineteen reports of complications of transfusion

were reported during the first three years of this surveillance system. The Table and Figure below show the nature, and relative frequency, of these reports.

**Table: Reports to SHOT, 1996-1999**

| Nature of complication | | Number | % of total |
|---|---|---|---|
| Incorrect blood transfused | IBT | 335 | 55% |
| Acute transfusion reaction | ATR | 89 | 14% |
| Delayed transfusion reaction | DTR | 82 | 13% |
| Post-transfusion purpura | PTP | 32 | 5% |
| Transfusion related acute lung injury | TRALI | 43 | 7% |
| Transfusion associated graft versus host disease | TA-GVHD | 12 | 2% |
| Transfusion transmitted infection | TTI | 19 | 3% |
| Unclassified | | 7 | 1% |
| Total | | 619 | 100% |

**Figure: Reports to SHOT, 1996-1999**




See Table above for key.

Twenty-six percent of these reports involved mortality of major morbidity associated with the transfusion complication. There was therefore 1 reported complication resulting in major morbidity or death for very 60,000 components issued for transfusion during these three years.

These data from the SHOT system, and similar data from other countries, provide evidence about how complications arise and present, and about the relative frequency of their presentation. However, under-recognition of complications associated with transfusion, and under-reporting usually mean the true number of complications is not known.

Either with or without a formalised reporting system, knowledge of the nature and causes of complications of transfusion is gained from the reporting of individual cases. Individual case histories are of particularly importance when new complications arise.

Increasingly - and particularly for the risks of transfusion transmitted infection - estimations of the number of expected complications are made by modelling the variables that give rise to complications.

Such estimations have now been published from many countries (Ref 4). In England it has been estimated that with anti-HCV testing in place (but in the absence of nucleic acid testing), less than 1 in 500,000 transfusions may be infectious for HCV and less than 1 in 3 million donations may be infectious for HIV. Higher, but broadly similar, estimates have been made in other developed countries. Estimates from some developing countries are orders of magnitude greater.

These estimates require certain assumptions to be made that may cause error in the results, and the resulting range of probable results can be very wide. It is difficult to validate these estimates and so there is always uncertainty around their accuracy.

Some risks are unknown, for example, the risk of vCJD from blood transfusion in UK. The approaches described above have not yet produced reliable knowledge about this risk - which leaves transfusion medicine specialists without any accurate risk assessments.

## Communication of this "professional knowledge"

John Paling in "Putting medical risks into perspective" (Ref 5) drew the distinction between data , information, knowledge and wisdom. Data are simply facts: transfusion services throughout the world abound in data collection. To take a simple example numbers of donations, sex of donors, age of donors etc. represent data .

Information is placing these facts in context: number of donations per population or per donor, movements in the numbers of donations with the day of the week or season etc.

Knowledge is bringing many fields of information together and, to continue with this particular example use of these donations and the adverse events associated with them related to other adverse events. We cannot have knowledge without information and we cannot have information without data.

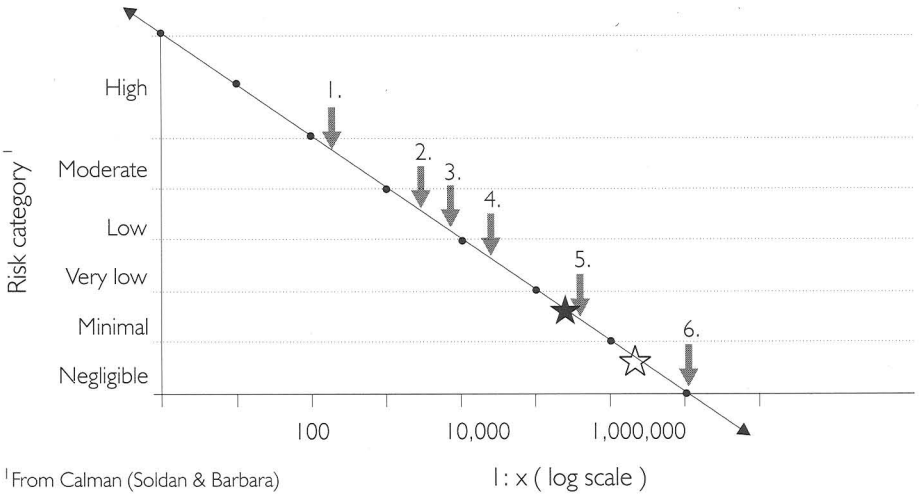
Wisdom, according to Paling, is non-context based understanding; a rare human trait.

Claudine Hossenlopp in communication about blood transfusion risks (Ref 6) points out that communication is always a two-way process. Otherwise it is merely a transfer of information. Communication involves checking the understanding of the recipient of the information. Risk communication is defined by Plough and Kirmsky (Ref 7)

as : experts intentionally conveying information about health or environment risks, obtained from scientists and technical experts, to a targeted audience of non-experts through designated channels.

Transfusion medicine specialists are used to talking of risks, such as 1 in 100, or 1 in 10,000 and seem to understand what this conveys . However it is clear that such facts mean little to the lay person and also the professional themselves when on the receiving end of a transfusion !.

There have been several attempts at communicating risk, not in numbers but pictorially. The SHOT pie chart is an example of such pictorial representation. Calman (Ref 8) published a risk line. We can use this to place the risk of transfusion in the context of other risks more familiar to people, as in the Figure below.




[1] From Calman (Soldan & Barbara)

Provisional estimates of infection in 1 donation:

☆ HIV

★ HCV

Death in 1yr due to:

1. Smoking 10 cigarettes / day
2. Influenza
3. Accident on road
4. Playing soccer
6. Hit by lightning

Paling has gone further and has developed a log diagram (Ref 5 and 9). The Paling Perspective Scale sets 0 at 1 in a million. This level has been chosen because it is the level below which all US government agencies have decided as a practical matter they will not regulate . Increasing and decreasing risks go logarithmically from this centre point, to the right and to the left respectively Most of us live comfortably with a " home base " of risks of between 1 in 10,000 and 1 in 100,000, although whether the risks are taken by choice or inflicted on us makes a great difference to acceptability. These charts are under continuing development and may become a useful tool in medicine.

Studies of public perception of risks of transfusion or donation are rare. Politis (Ref 10) found that in 1994 only 58% of a sample of 1995 answered the question " can you catch AIDS by giving blood ?" correctly ....

Finucane (Ref 11) collected data as part of a large national telephone survey of 1204 people in the US in 1997 and 1998. The results showed that a substantial proportion of the US population did not consider the US blood supply to be safe.

A seminar in London in October 2000 ( Transfusion 2020 ) explored this area further. The proceedings of this seminar will be published in Transfusion Medicine in early 2000.

## Options of risk reduction

The various options for risk reduction available to the transfusion services have been considered on an international level . (see diagram 1)

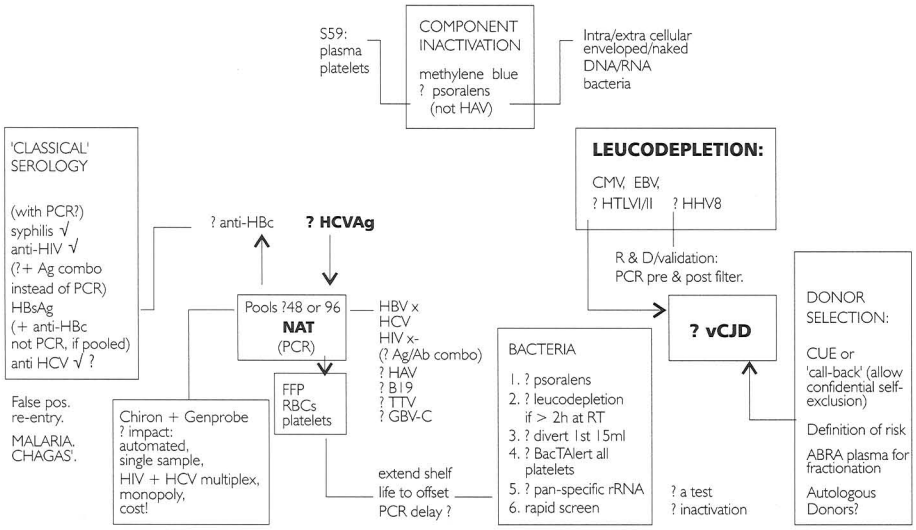
## Cost benefit debate in Transfusion Medicine

Transfusion Medicine specialists cannot escape becoming seriously involved in this debate in the 21st. Century . The extent of the debate throughout the transfusion chain were discussed by James and Barbara ( Ref 12 ) at an ESTM course in Castellanza in June 2000,

diagram 1

**Interacting Microbial Safety Options**

1. Need to define priorities and rank them
2. How many interventions to reduce each risk?




The WHO is currently addressing these issues at a global level with a Consultation on Blood safety Policies from an inter national perspective and attempting to develop a framework which will allow policy decisions to be based on clear assessments of costs and benefit and be applicable world wide.

Aubuchon (ref 13) has analysed cost and benefit of various medical interventions in terms of cost for each year of life extended by the intervention (see diagram 2).

diagram 2

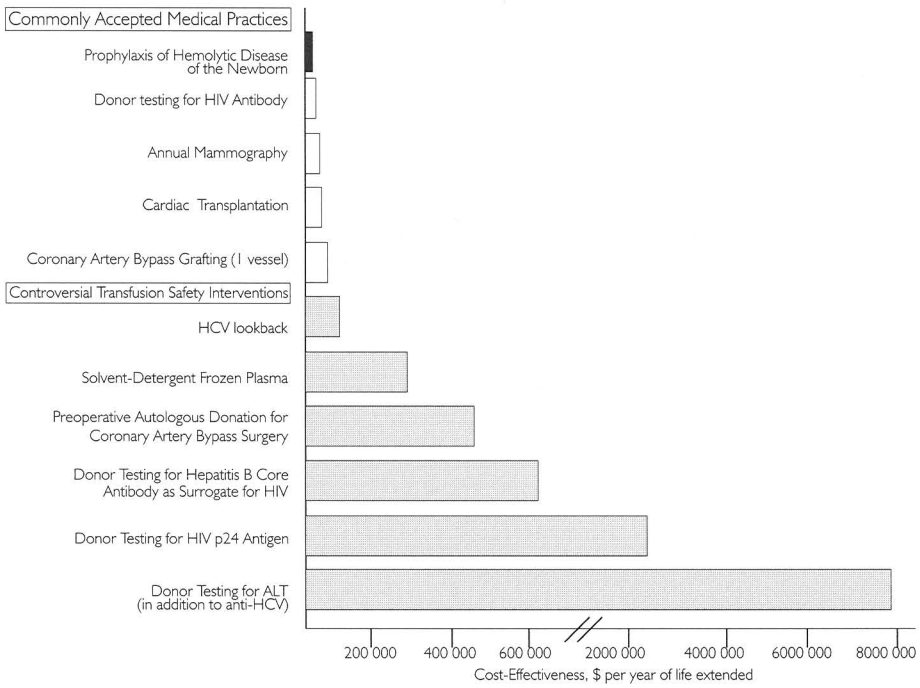



Figure 2. Comparison of cost-effectiveness of transfusion safety interventions (striped bars) and other medical practices (white bars) 27-31). ALT = alanine aminotransferase; anti-HCV = antibody to hepatitis C virus; HCV = hepatitis C virus.

(AuBuchon 1997, Ann Int Med 127, 904)

## Conclusion

Why does it matter to explore the public's perception of risk of blood transfusion in the 21st Century ?

Public acceptance of blood transfusion as a medical intervention is based on their perception of the risks involved. rather than the facts of the risk. It is clear that knowledge of the facts by the professionals is paramount , but this knowledge needs to be communicated to the public without distortion so they are able to make informed choices about their treatment . The future development of transfusion therapy, for example the development of blood substitutes depends on resources and anticipated demand , just as much as the development of commercial products. The demand comes from the public , and in this respect we must remember that the professionals are also part of the public.

Public acceptance of a certain level of risk of blood transfusion , if appropriately communicated may also influence the allocation of resources

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# Qality control and quality management of blood safety

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Transfusion medicine is a part of medical sciences. The primary objective of transfusion medicine is the treatment of patients with various blood components prepared from human blood.

Transfusion service prepares blood components from human blood by use of simple physical procedures. Blood components differ from the drugs manufactured by pharmaceutical industry.

The production of blood components is regulated by a special by-law. Blood components are not described in pharmacopeia. They differ from plasma derivatives and pharmaceuticals in a number of features. Very few blood components are made from a blood unit obtained from one individual blood donor. Each blood component is a single and unique lot. It is impossible to measure the potency of active substance, to determine the safety, toxicity, pyrogenicity and sterility, and to perform the procedure of virus inactivation in each blood component. In contrast, plasma derivatives are agents identical to the drugs manufactured by pharmaceutical industry, and they are described in pharmacopeia.

There are several definitions of quality. According to some of them, quality is described as fitness for use, fitness for purpose, or customer satisfaction (1). However, in transfusion medicine quality is defined as an adequate number of blood components for transfusion therapy, provided that blood components are efficacious and safe. Each link in the chain of blood preparation and transfusion treatment should meet the set requirements in order to achieve the required quality.

A number of different subjects is involved in the preparation of blood components and the transfusion treatment of patients. In Croatia, promotion of voluntary blood donation and donor selection is organized by the Red Cross and/or the transfusion service. Blood collection, laboratory testing, preparation, storage and release of blood components are completely in charge of the transfusion service. Transport and pretransfusion testing are organized by respective hospitals or hospital transfusion units or blood banks, while the ward physician, is the one responsible for the transfusion treatment of a patient. Thus, the responsibility for the preparation of blood components and for transfusion therapy is divided between a number of subjects, i.e. the Red Cross, transfusion units and hospitals. This may cause problems in the work, the more so, as neither the duties nor the responsibilities of each of the subjects have been well defined and demarcated, nor have any respective mutual agreements been made in writing. Such a situation entails difficulties in achieving the required quality of transfusion therapy, especially in solving misunderstandings that are due to transfusion side effects.

The quality of a blood product depends on the requirements set for the respective product, inherent features of each substance used in product preparation, technological characteristics of the laboratory or preparation process, the quality of work of the personnel involved, and the performance of critical steps in the process of blood component preparation or transfusion treatment of patients, i.e. it depends on the Red Cross or transfusion service promotion activities; transfusion service performance in blood collection and blood component preparation and pretransfusion testing; the work of the ward physician who is in charge of the patient treatment, such as transfusion therapy prescription, choice of a blood product, administration of blood transfusion, patient follow-up upon the completion of blood transfusion, and

identification and management of transfusion side effects. The desired quality is not always possible to achieve. Therefore, the requirements stated in the definition of transfusion treatment quality cannot always be met either. These considerations are exemplified below.

The required number of blood donors is ensured by promotion. The goal of blood donation promotion is to recruit donors without any form of risk behaviour, i.e. those free from an increased risk of blood products prepared from their blood being a cause of transfusion transmitted diseases. This goal is quite difficult to achieve, as undetected risk behaviour is still found in a relatively large percentage of blood donors and their blood may induce transfusion transmitted diseases in the transfused patient. For example, in 6% to 7% of all blood donors in the USA, the main reason for donating blood is testing for blood transmissible disease markers rather than a humanitarian motivation (2). In Germany, 10 of 186 examined donors were found to have used or to currently use narcotics at the time of the blood donation (3).

Neither blood donation promotion, nor donor selection, nor laboratory testing can detect all donors whose blood is infectious. Blood products prepared from the blood of an infected donor will cause transmission of the causative agent of transfusion transmitted diseases, with consequential infection of the majority of patients. Testing of blood donors certainly was and remains the most important procedure in reducing the risk of infection due to transfusion therapy. However, not even the most sophisticated laboratory testing can guarantee that the patient will not be infected with the viruses for the markers of which the donor has been tested, or with some other viruses, bacteria, or other agents found in the donor's blood, the presence of which has not been tested in the donor's blood. Laboratory testing can detect markers of infectious disease agents in the donor's blood only after a certain period of time has elapsed since his/her infection (the so-called window period). The time between the donor's infection and the occurrence of markers for transfusion transmitted diseases depends on the type of causative agent and the quality of the screening test used. This period is reduced by test improvement or by the introduction of new tests. However, even the best of tests currently used are burdened with a window period during which the donor's blood and blood preparations are infectious. Thus, with the introduction of NAT, the window period has been reduced from 29 to 11 days for HIV, from 59 to 34 days for HBV, and from 66 to 23 days for HCV (4). This is a real improvement in the safety of blood preparations concerning infection with most severe transfusion transmitted diseases; however, it only applies to the agents the blood is tested for, whereas other viruses, bacteria and other agents that may also cause transfusion transmitted disease remain undetected.

Improvement in the quality of testing in transfusion medicine has reduced the rate of morbidity and mortality due to transfusion therapy (5). Hepatitis and AIDS have ceased to be the most common risks of transfusion therapy, having been replaced by immune hemolytic reactions, bacterial infections, TRALI and GvHD as the main transfusion-related causes of death. The prevalence of ABO incompatibility has leveled off with the prevalence of hepatitis (5).

Critical points concerning blood product quality are also to be found in the process of blood product preparation. For example, in the Croatian Institute of Transfusion Medicine the training of the personnel and the performance modifications carried out from 1998 till 1999, reduced the number of ill welds in the device for sterile tube connection from 0.17% to 0.11%, the number of expired and discarded blood product units from 8.02% to 6.20%, the number of aggregates in platelet concentrates from 8.79% to 7.88%, the rate of package damage from 0.37% to 0.23%, and the rate of nonsterile platelet concentrates from 0.72% to 0.089% (6). In the year 2000, the favorable trend of the production quality improvement has continued, so that ill welds were observed in not more than 0.03%, platelet concentrate aggregates in 6.08%, and container damage in 0.24% of cases only (6).

Year by year, transfusion service provides clinicians with blood products of ever higher quality (7). In spite of this, the side effects and deaths due to transfusion therapy have been reported (8). In their study of the location of errors, Linden et al. (9) showed that the majority of reasons for post-transfusion side effects were generated at hospital locations of transfusion therapy use or in the interface between the transfusion laboratory and the clinical ward, rather than at the blood bank or transfusion centre (9). The cause of only 25% of post-transfusion reactions originated from a blood bank or a transfusion unit, and 17% were due to errors common to both the transfusion unit and the hospital ward (9). Accordingly, errors made at the hospital ward accounted for as many as 75% of post-transfusion reactions (9). The SHOT (serious hazards of transfusion) study of the causes of post-transfusion reactions from Great Britain has provided recommendations for the improvement of safety of the transfusion treatment (10). Most of these recommendations refer to the work at clinical departments.

The crucial question is whether a better quality of transfusion treatment can be achieved and if so, how to realize it. The quality is not incorporated in the product nor will it ensue by itself. The achievement of a desired quality level requires organized and systematic work on its improvement. Currently, it could be rephrased as the need for proper quality management.

There is a considerable lack of understanding, or a confusion among laymen and health professionals not closely engaged in the quality issues, concerning the terms quality control, quality assurance, quality system, and quality management. Therefore, definitions of these terms are given below, with a note that they differ according to the scope of activities and resources they involve. Quality assurance also includes all the procedures involved in quality control, while quality system includes both quality control and quality system.

Quality control defines operational techniques and activities that are used to fulfill requirements for quality (1).

Quality assurance defines all the planned and systematic activities implemented within the quality system and demonstrated as needed to provide adequate confidence that an entity will fulfill requirements for quality (1).

Quality system defines organization, structure, procedures, processes and resources needed to implement quality management (1).

Quality management defines all activities of the overall management function that determine the quality policy, objectives and responsibilities, and improvement means such as quality planning, quality control, quality assurance, and quality improvement within the quality system (1).

One of the most widely used quality systems in the world is ISO 9000 (1). It is expected to be soon substituted by ISO 2000. The system practically covers all fields of activities and work in the firm or organization except for accountancy, book-keeping, and some other administrative fields. According to this system, relationships between organizational units and among the people involved must be clearly explained, so that there is no overlapping of thear duties and responsabilities. Each individual process must be described. Every segment of the work with substantial impact on the product quality must be accompanied by written operation procedures. Workers should be properly educated to be able to follow the written operation procedures without deviations. Each result must be recorded, along with the name of the person who performed the work. Documentation must be regularly kept and stored according to in-house instructions or respective by-law. Instructions for work are modified upon analysis and evaluation of the results, and workers are re-educated to be able to follow the new ones. The objective of the system is to achieve such a level of the workers' performance which will be consistent with the written instructions for work,

thus producing uniform results of the work, avoiding errors, and controling changes in the work and the working process. The system cannot guarantee that errors will not occur; however, when an error does occur and its cause is identified, measures can be taken for the error not to recur, thus creating a spiral that yields a continuous quality improvement. The main goal of the quality system introduction is to influence the product quality. However, some other effects are also produced, e.g., reinforcement of the customer's or user's confidence, economic savings, etc.

Quality system management is achieved by defining organization and management responsabilities, education and training, analysis of work, analysis of nonconforming products and procedures and complaints, internal control, and implementation of corrective measures. The basis of successful system implementation is proper education of all workers and full adoption of the system by all the personnel involved.

ISO 9000 has been implemented at the Croatian Institute of Transfusion Medicine. To date, 52 procedures and 430 standard operating procedures, more than 170 specifications for starting material, intermediate and final products, and more than 300 various forms have been identified and described (6). The system implementation took several years; however, it has resulted in products of a considerably higher quality. The analysis of some inconsistencies has indicated that savings have already paid off the cost of the system introduction in the Croatian Institute of Transfusion Medicine.

The quality of transfusion therapy depends on a number of factors, and can only by influenced upon and improved by use of the quality system and quality management. Today, the critical location for quality of the transfusion therapy is the clinical ward and its interaction with the transfusion unit.

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# Who perspective on blood safety: The distance learning programme

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"The World Health Organization Blood Safety Unit (WHO/BLS) was established in 1994 to develop strategies for blood safety and promote them on a global, regional and national basis through advocacy and the provision of technical support to WHO member States." Dr. Jean C. Emmanuel, Chief, Blood Safety and Clinical Technology Unit, WHO.

Safe blood is one of the WHO stated priorities, enforced for the year 2000 by the World Health Day theme "Safe Blood starts with me/ Blood saves lives" (developed in conjunct action with the International Federation of Red Cross and Red Crescent Societies).

WHO data base on blood safety contains information from 167 countries. The world distribution of blood donations, blood testing and use has been analyzed for the interval 1997-1999, in relation with the Human Development Index (HDI). The criteria taken into consideration were life expectancy, education and medium income. Results show that more than 75 million blood units are collected annually, while the number of blood donors reported to 1000 inhabitants is 18 times higher in the countries with increased HDI, if compared to low (or medium) HDI countries.

The high cost procedures related to a quality blood transfusion practice and the constant need of national authorities involvement and governmental support, generated important discrepancies, especially in very poor countries, so that, presently 80% of the global population has access granted to only 20% of the safe blood reserve.

World Health Assembly Resolution 28.72/1975 urged member states to establish national blood transfusion services, based on voluntary non-remunerated blood donations. Due to lack of national coordination, only 35% of the 192 member states have now a national blood transfusion policy, a legal frame and a specific structure responsible for the national blood programme. This has been used as a major point for elaborating guidelines, recommendations in order to support and develop a global strategy for a safer blood.

Only a structured and well-organized blood transfusion service can provide the necessary supplies of safe blood. WHO strategy for blood safety considers systematic control of blood donors and blood products as essential, but not enough as a safe blood guarantee. In this respect, 4 key issues are emphasized, covering the blood transfusion chain:

- establishment of a nationally coordinated blood transfusion service, with adapted legal frame;
- blood collection from voluntary non-remunerated blood donors only (low-risk populations) selected by rigorous medical criteria (A system based on voluntary and regular blood donations enables a more efficient use of limited resources, by minimizing the ratio of discarded products.);
- screening all donated blood for transfusion transmissible infections and immuno-hematology using the most appropriate tests available, good laboratory practice in all aspects of blood processing;
- reduction of unnecessary transfusions and increasing transfusion therapy efficacy (adequate clinical use of blood).

Quality, the 5th main target should be present at every level, including the aspects of global management and policy.

As a pertinent tool for local training, up-dating and use of international recommendations on blood safety, WHO initiated the distance learning materials, specially designed and supplied directly to individual learners. This type of educational programme is part of WHO strategy to support national training initiatives on blood safety. It provides ongoing tutorial, guidance and supervised practical training. It can also be adapted to fit professional commitments and individual learning requirements, considering the variation of training needs of staff working at different levels of the BTS.

The BTS distance learning materials: "Safe blood and blood products", have been translated by now in Russian, Arabic, Spanish, Portuguese, Romanian, Chinese and Farsi.

The modules cover the following subjects:

- Introductory module: Guidelines and principles for safe transfusion practice;
- Module 1: Safe blood donation;
- Module 2: Screening for HIV and other infectious agents;
- Module 3: Blood group serology;
- Trainer's guide;
- Establishing a distance learning programme in blood safety: a guide for programme coordinators.

In 1999, the "Costing of Blood Transfusion Services" (financial management of the BTS) has been released, while the "Clinical use of Blood" (module + pocket handbook) and "The Blood Cold Chain' (guide for managers and users) are under preparation.

The aims of the whole distance learning project are to:

- update knowledge;
- improve technical skills and performance;
- strengthen understanding and abilities;
- encourage evaluation of personal and general practice;
- identify errors and ways of correction and improvement.

The target audience is represented by all actors involved in transfusion medicine:

- propaganda officers: in charge with pro-donation education, donor recruitment, motivation and retention;
- laboratory technical staff: in blood transfusion centers, hospitals, public health laboratories;
- teaching staff: senior professionals involved in training programmes, in blood transfusion services, universities, other training institutions;
- medical/ paramedical staff: wishing to know more.

The learner support system involves trainers, responsible for facilitating and training, and supporters: responsible for providing individual guidance, feedback and support at local level. A national coordinator is necessary for programme management.

In practical terms, an increased number of staff can have access to training. The modular structure of the materials accommodates to various degrees of knowledge, becoming a "build on" process of learner's individual experience.

The whole learning process is more cost-effective (fewer trainers, reduced staff absence, in service training) compared to other educational programmes. In the same time, the constant use of training materials written by international experts, with reference to generally accepted recommendations, promotes uniformity in approach and standardization of procedures.

Supported by health authorities and carefully planned, a distance learning programme can become an important tool in increasing awareness, developing and strengthening staff abilities for a safer transfusion practice.

The WHO initiative – creating specific distance learning materials, offers a flexible and cost effective issue for extensive training and improved quality approach in transfusion medicine.

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# Tveganje in varnost anestezije

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## Uvod

Kljub vedno bolj zapletenim in obsežnim operacijam, tudi pri bolnikih z več spremljajočimi boleznimi, se je pogostnost obolevnosti in umrljivosti kot posledica anestezije v zadnjih 50 letih močno zmanjšala. Danes le redko nastanejo hudi zapleti ali smrt zaradi anestezije. Na dokazano izboljšanje anestezijske prakse, ki se odraža v bistveno zmanjšanem številu zapletov pri anesteziji, je odločno vplivalo uveljavljanje strokovnih standardov pri strokovnem usposabljanju, pri izboru in uporabi opreme ter pri uvajanju novih učinkovin, veščin in postopkov za optimalno vodenje anestezije. Dosežena raven anestezijske stroke nam danes omogoča uspešno anestezirati tudi zelo mlade (nedonošenčke), zelo stare (tudi nad 100 let)(1) in zelo hudo bolne. Večino takih bi še pred 30 leti ocenili kot neprimerne za anestezijo.

## Zapleti v povezavi z anestezijo

Prvo pisno poročilo o 16 smrtnih zapletih v povezavi z anestezijo je objavila francoska akademija za znanost in medicino leta 1847 (2), eno leto potem, ko je Morton v Bostonu prvič na svetu demonstriral anestezijo z etrom.

V študiji iz leta 1954 Beecher in Todd (3) poročata za obdobje od 1948 do 1952 o enem smrtnem primeru na 2600 anestezij. V začetku osemdesetih (4,5) se je to tveganje zmanjšalo na en smrtni zaplet na 10.000 operacij, v drugi polovici desetletja pa od 1 primera na 13.207 operacij do 1 primera na 185.000 operacij (6). Proučevanja smrtnih zapletov so pokazala, da so bili glavni vzroki zanje nepravilna ocena bolnikovega stanja pred anestezijo in operacijo ter pomanjkljiv med- in pooperativni nadzor (6). Pri natančnejših analizah anestezijskih zapletov so ugotovili, da je bil čas od prvih znakov anesteziološkega zapleta do razvoja kritičnega stanja pri bolniku dovolj dolg za prepoznavo vzroka, ki je zaplet povzročil in tudi za njegovo razrešitev (7). Za tovrstno ukrepanje pa je seveda potrebna odgovarjajoča oprema za nadzor življenjskih funkcij (8).

Eichhorn in sodelavci (9) so primerjali število hudih anesteziooloških zapletov pri dveh skupinah bolnikov v harvardskih bolnišnicah. V obdobju med 1976-85 letom so pri

Tabela 1: Najpogostejši vzroki hudih zapletov pri anesteziji
*(Aitkenhead AR, 3rd ESA Congress, Paris 1995:Refresher Course Lectures:RC-2)*

| Zapleti z dihalnim sistemom: | Zapleti pri intubaciji in nadzoru dihalnih poti: |
|---|---|
| • Odklop | • Neuspela intubacija |
| • Nepravilna spojitev | • Intubacija v požiralnik |
| • Puščanje | • Intubacija v bronh |
| | • Prezgodnja ali nehotena ekstubacija |
| | • Aspiracija |
| **Zapleti pri dajanju učinkovin:** | **Okvare v opremi:** |
| • Preveliki odmerki | • Laringoskopov |
| • Premajhni odmerki | • Infuzijskih črpalk |
| • Uporaba napačne učinkovine | • Dihalnih sistemov in nepovratnih valvul |
| | • Aparatov za nadzor življenjskih funkcij |

757.000 bolnikih, vključenih v študijo, ugotovili 10 hudih zapletov in 5 smrti. Po letu 1985, ko so uvedli standarde za minimalni medoperativni monitoring, pa so pri 244.000 anestezijah imeli samo en hud zaplet in nobene smrti.

Najpogostejši resni zapleti, ki se dogajajo v povezavi z anestezijo, so prikazani v tabeli 1.

Študije (10-14), ki so proučevale, v kolikšni meri so na nastanek hudih zapletov pri anesteziji vplivale človeške napake in okvare na anestezijski opremi, so pokazale, da se razmerje teh dveh dejavnikov v obdobju od sredine 1970 do sredine 1990 ni spremenili.

Tabela 2: Človeške napake in okvare v opremi (10-14)

| Študija | Obdobje | Štev. hudih zapletov | Človeška napaka (%) | Okvara v opremi (%) |
|---|---|---|---|---|
| 10 | 1975-1980 | 1089 | 71 | 17 |
| 11 | 1978 | 359 | 82 | 14 |
| 12 | 1981 | 82 | 68 | 20 |
| 13 | 1989-1990 | 549 | 75 | 21 |
| 14 | 1993 | 2000 | 83 | 12 |

V zadnjih 10. do 15. letih se je močno povečala uporaba področne anestezije. V prospektivni študiji o zapletih pri podroèni anesteziji, ki je bila nedavno narejena v Franciji (15), poročajo, da je pri izvedbi 103.730 področnih anestezij (40.640 subarahnoidnih, 30.413 epiduralnih, 21.278 perifernih živčnih blokad in 11.229 intravenskih področnih anestezij) prišlo do 28 hudih zapletov (Tabela 3).

Tabela 3: Število hudih zapletov v povezavi s področno anestezijo (15)

| | Področna anestezija | | | | |
|---|---|---|---|---|---|
| Hudi zapleti | Sub-arahnoidna (40.640) | Epiduralna (30.413) | Bloki perifernih živcev (21.278) | Intravenska področna (11.229) | Skupaj (103.730) |
| Srčni zastoj | 26<br>(6.4)<br>(3.9-8.9) | 3<br>(1.0)*<br>(0..2-2.9) | 3<br>(1.4)**<br>(0.3-4.1) | 0<br>-<br>(0-3.3) | 32<br>(3.1)<br>(2.0-4.1) |
| Smrt | 6<br>(1.5)<br>(0.3-2.7) | 0<br>-<br>(0-1.2) | 1<br>(0.5)<br>(0-2.6) | 0<br>-<br>(0-3.3) | 7<br>(0.9)<br>(0.2-1.2) |
| Krči | 0<br>-<br>(0-0.9) | 4<br>(1.3)<br>(0.4-3.4) | 16<br>(7.5)***<br>(3.9-11.2) | 3<br>(2.7)<br>(0.5-7.8) | 23<br>(2.2)<br>(1.3-3.1) |
| Nevrološke okvare | 24<br>(5.9)<br>(3.5-8.3) | 6<br>(2.0)*<br>(0.4-3.6) | 4<br>(1.9)***<br>(0.5-4.8) | 0<br>(2.7)****<br>(0.5-7.8) | 34<br>(3.3)<br>(2.2-4.4.) |
| Okvare živčnih korenov | 19<br>(4.7)<br>(2.6-6.8) | 5<br>(1.6)*<br>(0.5-3.8) | 4<br>(1.9)<br>(0.5-4.8) | 0<br>-<br>(0-3.3) | 28<br>(2.7)<br>(1.7-3.7) |
| Sindrom kaude ekvine | 5<br>(1.2)<br>(0.1) | 0<br>-<br>(0-1.2) | 0<br>-<br>(0-1.7) | 0<br>-<br>(0-3.3) | 5<br>(0.5)<br>(0.2-1.1) |
| Paraplegija | 0<br>-<br>(0-0.9) | 1<br>(0.3)<br>(0-1.8) | 0<br>-<br>(0-1.7) | 0<br>-<br>(0-3.3) | 1<br>(0.1)<br>(0-0.5) |

*= razmerje epiduralna proti subarahnoidni anesteziji
** = razmerje periferni živčni blok proti spinalni anesteziji ($p<0,05$)
*** = razmerje periferni živčni blok proti epiduralni anesteziji ($p<0,05$)
**** = razmerje intravenska področna proti epiduralni in subarahnoidni anesteziji ($p<0,05$)

Najpogostejši zaplet je bil zastoj srca. Do tega je prišlo pri 32 bolnikih, 7 od njih jih je za posledicami zastoja umrlo. Do srčnega zastoja je prišlo v glavnem v povezavi s subarahnoidno anestezijo (6,4±1,2 na 10.000 bolnikov), pri epiduralni in periferni blokadi živcev skupaj pa je bilo zastojev pomembno manj (1,0±0,4 na 10.000 bolnikov). Velik odstotek srčnih zastojev v povezavi s področno anestezijo v tej študiji avtorji bolj povezujejo z vrsto operacije in spremljajočimi obremenilnimi dejavniki, kot so visoka starost in razna dodatna obolenja, manj pa z izborom področne anestezije. V študiji so zaznali nevrološke zaplete pri 34 bolnikih. Od tega so bile pri 29 bolnikih nevrološke okvare prehodne narave in so se v razdobju od 48 ur do 3 mesecev popravile. Pri petih bolnikih so nastale trajne nevrološke okvare, tako so označili tiste, ki se po treh mesecih še niso popravile. Tudi pogostnost nevroloških zapletov je bila pri subarahnoidni anesteziji večja (6±1 na 10.000 primerov) kot pri epiduralni, intravenski področni anesteziji in blokadi perifernih živcev skupaj (1,6±0,5 na 10.000 primerov). Pri bolnikih, ki so dobili subarahnoidno anestezijo, so ugotovili relativno tveganje (4,7 na 10.000 primerov), za okvare živčnih korenov in 1,2 na 10.000 primerov za sindrom kaude ekvine. En bolnik iz te študije, ki je dobil epiduralno anestezijo, je postal paraplegičen. Računalniška tomografija pri njem ni pokazala patološkega izvida. Med operacijo je ta bolnik utrpel hudo hipovolemično arterijsko hipotenzijo, ki je verjetno povzročila ishemijo hrbtenjačnega mozga in posledično paraplegijo. Krče zaradi povečane koncentracije lokalnega anestetika v krvi so opazili najpogosteje po blokadi perifernega živca (relativno tveganje 7,5 na 10.000 primerov), manjkrat po intravenski področni anesteziji (relativno tveganje 2,7 na 10.000 primerov) in najredkeje po epiduralni anesteziji (relativno tveganje 1,3 na 10.000 primerov).

Študijo o zapletih pri subarahnoidni in epiduralni anesteziji so pred nedavnim izvedli tudi na Finskem (16). V obdobju od 1987 do 1993 so naredili 550.000 subarahnoidnih in 170.000 epiduralnih anestezij. Na osnovi odškodninskih zahtevkov bolnikov so ugotovili, da je bila pogostnost nevroloških zapletov 1,8 na 10.000 subarahnoidnih anestezij in 2,4 na 10.000 epiduralnih anestezij. Epiduralni hematom je bil diagnosticiran pri 5 bolnikih, pri vseh po subarahnoidni anesteziji. Pri enem bolniku je po epiduralni anesteziji prišlo do paraplegije. Izvedba te anestezije je bila tehnično zelo težka, saj je bilo potrebno več vbodov in prišlo je tudi do punkcije dure pred vstavitvijo katetra. Pri bolniku so naredili mielografijo, ki ni pokazala patoloških sprememb. Ocenili so, da so vzročni dejavniki za nastanek paraplegije verjetno epiduralna anestezija v povezavi z bolnikovo aterosklerozo in posledično ishemijo hrbtenjačnega mozga. Sindrom kaude ekvine so diagnosticirali pri dveh bolnikih, pri enem po subarahnoidni in pri drugem po epiduralni anesteziji. Pri bolniku, ki je dobil subarahnnoidno anestezijo so po posegu diagnosticirali zožitev hrbtenjačnega kanala zaradi spondiloartroze, pri bolniku z epiduralno anestezijo pa niso našli nobenega dejavnika tveganja za nastanek tega sindroma. Sindrom kaude ekvine se je razvil prvi pooperativni dan, potem ko so bolniku odstranili epiduralni kateter.

Rezultati o zapletih pri področni anesteziji kažejo, da je tako kot pri izvajanju splošne anestezije, tudi pri področni anesteziji zelo pomembno upoštevati standarde za varnost bolnikov po anesteziji, ki jih moramo dovolj dolgo nadzorovati, da pravočasno prepoznamo morebitne zaplete in odgovarjajoče ukrepamo.

## Ali z izbiro anestezijske tehnike lahko vplivamo na kakovost pooperativnega izida?

Številne študije, ki so bile narejene v zadnjem desetletju, so pokazale, da na kakovost pooperativnega izida poleg kirurških dejavnikov odločilno vpliva tudi priprava bolnika na anestezijo in operacijo, izbira anestezijske tehnike, vzdrževanje homeostaze med operacijo in po njej, vključno z zdravljenjem pooperativne bolečine (17,18,19,20).

Ena od pomembnih nalog anesteziologa je predoperativni pregled in ocena bolnika z namenom, da ugotovi pripravljenost bolnika na anestezijo in operacijo, ali po potrebi svetuje še dodatno pripravo. Na osnovi takega pregleda se odloči za anestezijsko tehniko, ki bo za bolnika najprimernejša ter predvidi ustrezni pooperativni nadzor in zdravljenje, vključno z odgovarjajočim načinom zdravljenja pooperativne bolečine.

Kirurški posegi, še posebej obsežni in dolgotrajni, preko simpatičnega in somatskega živčnega sistema sprožijo izločanje nevroendokrinih hormonov (adrenokortikotropni, antiduretični, rastni, tireoideostimulirajoči hormon, adrenalin, noradrenalin, kortizol, aldosteron, renin), lokalno iz poškodovanega tkiva pa citokine (interlevkin 2 in 6, tumorski nekrotizirajoči faktor). Vsi ti posredniki pri bolniku povečujejo presnovo, utrip srca, nagnjenost k strjevanju krvi in delujejo zaviralno na imunski sistem, kar ima lahko negativne posledice na delovanje enega ali več organov, še posebej pri bolnikih s predhodnimi boleznimi (21,22,23).

Kehlet (22) je postavil hipotezo, da bi neželene posledice stresa zaradi operacije lahko zmanjšali, če bi uspeli zavreti odgovor organizma na kirurški stres. S širjenjem spoznanja o škodljivem učinku kirurškega stresa na organizem, se je tudi pozornost anesteziologov usmerila v iskanje načinov kako z anestezijsko tehniko omiliti njegove posledice.

## Obolevnost srca v perioperativnem obdobju

Obolevnost srca med operacijo in po njej se najpogosteje pokaže v obliki srčnega infarkta, angine pektoris, srčnega popuščanja ali življenjsko nevarnih motenj srčnega ritma. To so tudi najpogostejši vzroki za pooperativno umrljivost. Perioperativni stres z aktivacijo simpatičnega živčevja povečuje potrebo po kisiku v srčni mišici. Sočasno pa aktivacija srčnih simpatičnih živcev pri bolnikih z aterosklerotičnimi zožitvami venčnih arterij lahko sproži paradoksno vazokonstrikcijo teh. Paradoksna vazokonstrikcija še dodatno zmanjša dovod kisika v tisti del srčne mišice, ki se nahaja distalno od zožitve. Neuravnotežena oskrba s kisikom povečuje tveganje za nastanek ishemije srčne mišice in nastanek srčnega infarkta, in se odraža v višji stopnji pooperativne srčne obolevnosti in smrtnosti (24,25,26). Raziskave na živalih in na ljudeh so pokazale pozitiven učinek torakalne epiduralne anestezije na delovanje srca in paradoksno vazokonstrikcijo venčnih arterij (47,48,49). Za operacije na srcu so Tenling in sod. (45) ugotovili, da dodatek epiduralne anestezije splošni anesteziji omogoča hitrejšo ekstubacijo bolnika po operaciji, kakor tudi vzdrževanje normalnega ventilacijsko perfuzijskega ravnovesja in oksigenacije v pooperativnem obdobju.

Yeager in sod. (27) so prikazali, da kombinacija splošne anestezije z epiduralno anestezijo zmanjša pooperativno obolevnost in smrtnost pri bolnikih, ki so imeli obsežne operacije v trebušni in prsni votlini ali na žilju in so bili uvrščeni v skupino zelo rizičnih kirurških bolnikov. Nadaljnje študije, ki so obravnavale podobno problematiko, so prišle do nekonzistentnih rezultatov. Verjetno zaradi razlik v načrtovanju študij, pri izbiri bolnikov in v trajanju ter obliki zdravljenja pooperativne bolečine (28,29,30,31).

## Strjevanje krvi

Perioperativni stres povzroča zvečanje strjevanja krvi v pooperativnem obdobju in s tem večje tveganje za nastanek trombemboličnih zapletov (32). Ugotovili so, da epiduralna analgezija preko številnih mehanizmov zmanjšuje nagnjenost k povečanju strjevanja krvi v pooperativnem obdobju (33,34). Tuman in sod. (30) navajajo pomembno zmanjšanje pooperativnih tromboz žilnih transplantatov pri bolnikih, ki so imeli analgezijo med operacijo za vstavitev žilnih transplantatov, kakor tudi po njej, zagotovljeno po epiduralni

poti. Do podobnih ugotovitev je prišel tudi Christopherson s sod. (35). Imeli so manj reoperacij zaradi trombemboličnih zapletov po žilnih operacijah na spodnjih okončinah pri tistih bolnikih, ki so dobili epiduralno analgezijo.

## Pljučni zapleti

Po operacijah v prsni in trebušni votlini se pljučne funkcije močno zmanjšajo. Negativni stranski učinek teh operacij se najbolj odraža v zmanjšanju funkcionalne rezidualne kapacitete (FRK) in zmanjšanju delovanja diafragme (zaradi refleksne zavore preko nervusa frenikusa). Zaradi zmanjšane FRK pride do tvorbe atelektaz, ventilacijsko-perfuzijskega neujemanja, hipoksemije in pljučnice. Splošna anestezija z uporabo mišičnih relaksantov in inhalacijskih anestetikov, opioidov in nadzorovanega predihavanja tudi prispeva k zmanjšanju pljučnih funkcij. Bistveno manjši negativni vpliv na te funkcije naj bi imela torakalna epiduralna anestezija. Pri zmanjševanju pooperativnih pljučnih zapletov ima pomembno vlogo pooperativna epiduralna analgezija, ker zagotavlja boljšo analgezijo, izboljša delovanje diafragme in zmanjšuje pogostnost nastanka hipoksemije (32).

Po pregledu obsežne literature Liu in sod. (32) ugotavljajo, da sta epiduralna anestezija in analgezija predvsem pomembno prispevali k zmanjšanju pooperativnih pljučnih zapletov pri bolnikih z velikim tveganjem za nastanek teh zapletov (debeluhi, stari, predhodne pljučne bolezni, obsežne operacije v trebušni in prsni votlini).

## Pooperativno delovanje prebavil

Pooperativni ileus je začasno poslabšanje peristaltike prebavil. Čeprav se najpogosteje in v najtežji obliki pojavi po operacijah v trebuhu, se pojavlja tudi po drugih operacijah. Ena od teorij o nastanku ileusa pravi, da abdominalna bolečina aktivira spinalni refleksni lok, ta pa zavre peristaltiko črevesja. Povečano simpatično draženje črevesja zaradi kirurškega stresa še dodatno zmanjšuje njegovo peristaltiko. Domnevno velja, da glavno vlogo pri nastanku ileusa igrajo aferentni nociceptivni in eferentni simpatični živci. Pomemben dodatni dražljaj za nastanek ileusa je tudi ishemija črevesja. Številne klinične študije so pokazale, da pooperativna epiduralna analgezija z uporabo lokalnega anestetika skrajša trajanje pooperativnega ileusa v primerjavi z analgezijo, ki jo dosežemo z dajanjem opioidov intravensko ali intramuskularno. Prav tako je bilo pooperativno okrevanje črevesja hitrejše kadar so bolniki dobili opioide po epiduralni poti, v primerjavi z intravenskim načinom. Prednost uporabe lokalnih anestetikov pred opioidi bi lahko bila v tem, da lokalni anestetik ne blokira samo bolečinske poti, ampak tudi simpatično živčevje, ki oživčuje prebavni trakt (32). V novejšem, preglednem članku o vplivu epiduralne anestezije na prebavila, so poudarili, da je za uspešno okrevanje črevesja pomembno mesto izvajanja epiduralne blokade (36). S torakalno epiduralno blokado so pospešili okrevanje črevesne peristaltike, z lumbalno epiduralno blokado pa niso bili tako uspešni. Razlaga za tak izid zdravljenja bi lahko bila povečana aktivnost simpatičnega živčevja v neanesteziranih predelih splanhničnega področja po lumbalni epiduralni anesteziji (37).

## Kognitivne funkcije

Prehodne pooperativne spremembe v kognitivnih funkcijah so splošen pojav pri vseh operirancih, vendar slabo pojasnjen. Kognitivne funkcije so pogosteje zmanjšane pri starostnikih (10-50%). Višek poslabšanja kognitivnih funkcij nastopi drugi dan po operaciji. Za popolno okrevanje je običajno potrebno teden dni, pri starejših pa lahko

tudi mesec dni. Poslabšanje mentalnih funkcij pri starejših je tesno povezano z večjo pogostnostjo zapletov, kot so depresija, možganska kap, preležanine, urološki zapleti in z odloženo vrnitvijo v domače okolje (32). Hole s sod. (38) je ugotavljal mentalno stanje bolnikov po operacijah kolka, ki so bile narejene v splošni in epiduralni anesteziji. Mentalno stanje bolnikov, ki so dobili epiduralno anestezijo je bilo bistveno boljše kot pri tistih, ki so dobili splošno anestezijo. V nadaljnjih študijah (39,40,41,42) so bolnike razdelili v tri skupine: v prvi so dobili samo epiduralno anestezijo, v drugi samo splošno in v tretji kombinacijo epiduralne in splošne anestezije. Rezultati so pokazali zelo podobne pooperativne spremembe kognitivnih funkcij pri vseh treh skupinah in se niso pomembno razlikovali glede na vrsto anestezije.

## Multimodalno pooperativno zdravljenje

Kehlet (22) ugotavlja, da je bilo doslej vloženih veliko naporov v zmanjševanje pooperativne obolevnosti in umrljivosti s posameznimi anestezijskimi tehnikami, kot sta npr. epiduralna anestezija in analgezija, vendar so ugotovljeni pozitivni vplivi na izboljšanje pooperativnega izida še vedno predmet strokovnih razprav. Številni zagovarjajo širši, kombinirani, tim. multimodalni pristop. Moiniche s sod. (43) poroča, da so pri bolnikih, ki so bili operirani na debelem črevesu skrajšali bivanje v bolnišnici, potem ko so uporabili kombinirano uravnoteženo analgezijo, zgodnje hranjenje skozi usta in hitro mobilizacijo bolnika. Brodner s sod. (44) je preučeval multimodalni pristop pri bolnikih, ki so bili operirani na požiralniku s torako-abdominalnim pristopom. Bolniki so med operacijo poleg splošne anestezije dobili še epiduralno anestezijo in pooperativno epiduralno uravnoteženo analgezijo. Epiduralni odmerki učinkovin so bili prilagojeni individualno glede na potrebe posameznega bolnika, vse bolnike so tudi kmalu po operaciji ekstubirali in hitro mobilizirali. Pri teh bolnikih so ugotovili uspešnejše zdravljenje bolečine, manjšo negativno dušikovo bilanco in hitrejše odpuščanje iz enote za intezivno zdravljenje v primerjavi z bolniki, ki so med operacijo dobili splošno anestezijo in pooperativno epiduralno analgezijo brez dodatnega rehabilitacijskega programa.

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# Varna transfuzija krvi
# Safe blood transfusion

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## Uvod

Marsikdo se rad poigra z besedami in postavi vprašanje: koliko varnosti je zadosti za varno transfuzijo? Popolne ali 100% varnosti ni in je ne bo, zato vedno tehtamo in nihamo med dobrobitmi in morebitnimi stranskimi negativnimi učinki. Pojem varnosti ima različno težo v različnih okoljih in posameznih družbah. Pojmovanje varnosti se tudi spreminja s časom in novimi dognanji. Posamezniki in tudi posamezne skupine ljudi dajejo pojmu varnosti različen pomen. Pojem varna transfuzija dobiva posebno težo znotraj težnje po višji stopnji zdravstvenega varstva in širše težnje po varnem življenju. Na ukrepe za varno transfuzijo krvi pa ima poleg strokovnih spoznanj in finančnih zmožnosti, ki sta bila v preteklosti osnova za vsak ukrep, vedno večjo vlogo javno mnenje in z njim povezane politične odločitve.

## Zgodovinski pregled

V preteklosti smo na področju varne transfuzije krvi postopno vključevali različne postopke in ukrepe v glavnem na dveh področjih: pri izbiri krvodajalca in na področju testiranja krvi.

Vsi ukrepi so temeljili na takratnih strokovnih spoznanjih. Kasneje je moral biti učinek na osnovi strokovnih spoznanj v sprejemljivem razmerju do izdatkov. Finančna presoja je bila v različno razvitih sredinah različna. Razvite države Evrope in Amerike so praviloma prve vpeljevale obsežnejše in dražje rešitve. V zadnjih letih, ob pojavu AIDSa in še posebno ob pojavu spongiformne encefalopatije pri govedu in pojavu prionov pri ljudeh, je ob povečanem pritisku javnosti v Angliji prvič sprejeto stališče, da ne moremo čakati na izsledke stroke in na ustrezne strokovne predloge, temveč moramo ukrepati takoj. Odprli smo neizmerno široko polje političnih odločitev, ki postavljajo strokovne odločitve v ozadje.

## I. Krvodajalci

Vir krvi so krvodajalci, zato je Svetovna zdravstvena organizacija posvetila dan zdravja krvodajalcem in v prenesenem pomenu zdravnikom, z geslom "Safe blood starts with me". Krvodajalstvo mora temeljiti na prostovoljnosti in neplačanosti. Obenem moramo spoznati, da le dobra četrtina držav v svetu lahko nudi zadostne količine varne krvi, med njimi je tudi Slovenija.

1) Osnovni pogoj za varno kri, je dobra informiranost krvodajalcev in javnosti, s čimer omogočimo bodočim krvodajalcem možnost **samoizključitve**.
2) Drugi ukrep je **konsultacija** krvodajalca s šolanim zdravstvenim osebjem, ki zajema dve področji: a) objektivno ugotavljanje zdravja in b) zajemanje epidemioloških podatkov oziroma ugotavljanje načina življenja krvodajalca.

a) Postopek ugotavljanja zdravstvenega stanja zajema presojo objektivnih izsledkov kot so laboratorijski izvidi, krvni pritisk, srčna akcija, splošni zdravniški pregled itn.

b) Drugi sklop pa je anamneza – zbiranje epidemioloških podatkov, ko krvodajalec pove dogodke po svoji presoji. Po lastni presoji nam krvodajalec pove svoje videnje preteklih dogodkov preko vprašalnika in po potrebi tudi ustno. Pozorni smo na epidemiološke podatke vezane na presojo zdravstvenega stanja oziroma, ali potencialni krvodajalec pripada skupini ljudi, ki je bolj izpostavljena določenim okužbam. Več bolezni se prenaša ob spolnem kontaktu, zato so pomembni tudi podatki o spolnih navadah. Od leta 1985 smo dali poseben povdarek, zbiranju teh podatkov ob spoznanju, da se lahko prenaša HIV tudi s transfuzijo okužene krvi in krvnimi pripravki. Vsi napori v zvezi z zbiranjem podatkov temeljijo na predpostavki odgovornega odnosa krvodajalca in prisotne družbene zavesti, kar pa ni vedno res, saj se skupine posameznikov, ki živijo na svojstven, bolj ali manj tvegan način, pogosto nahajajo na robu družbenih normativov in jim ni mar za družbene vrednote. Temu primerna je tudi pričakovana kakovost odgovorov. Pri pismenem vprašalniku so vsa vprašanja standardizirana in dobijo vsi krvodajalci ista vprašanja, ki so obenem dokumentirana, kar je sigurno bistvena prednost in izpoljnujemo osnovne zahteve kontrole kakovosti, zavedamo pa se, da smo tako odpravili individualni pristop. Izobrazbena raven krvodajalcev je različna in tako naletimo na drugo težavo kako pripraviti razumljiv in učinkovit vprašalnik. V zadnjem obdobju srečujemo v javnosti vedno več vprašanj o prionih in ukrepih za preprečevanje širjenja leteh. Večini krvodajalcev so prioni in obolenja povezana z njimi neznanka in tako je zopet močno pridobilo na veljavi stalno in kakovostno informiranje.

## 2. Uvedba testov

Kri je biološki material, ki je potencialno kužen, čeprav izvira od zdravih krvodajalcev saj v medicini poznamo pojem zdrav prenašalec. Rezultati testov spadajo med objektivne pokazatelje kazalcev okužbe, ki pa na žalost niso vedno zadosti občutljivi.

Različne teste smo uvajali glede na dostopnost, učinkovitost, glede na lokalno epidemiološko situacijo, strokovno presojo in ceno testa.

Prvi test, ki smo ga uporabili pri izbiri primerne krvi za transfuzijo, je bil že v zgodnjih petdesetih letih vpeljan test na ugotavljanje prisotnosti povzročitelja sifilisa.

Zaradi spoznanja, da se v tistem obdobju tako imenovani serumski hepatitis prenaša s krvjo, so po svetu uvedli leta 1965 test na ALT ( jetrni test na alanin aminotransferaze), ki sicer ni specifičen test za hepatitis, vendar lahko indirektno pokaže ob prizadetosti jeter tudi na nevarnost prenosa hepatitisa. Vse krvodajalce smo začeli testirati na prisotnost HBsAg (površinski antigen hepatitis B virusa ) leta 1970. Uvedba testiranja vsakega odvzema krvi je dramatično znižala prenos hepatitisa B s krvjo.

Najbolj odmevno je bilo uvajanje testiranja na prisotnost protiteles proti povzročitelju AIDSa. V Sloveniji smo uvedli postopek testiranja leta 1986.

Daleč manj odmeven je bil začetek testiranja na protitelesa proti HC ( hepatitisu C ) leta 1993, kljub temu, da je v Sloveniji okoli 0,3% pozitivnih krvodajalcev oziroma, da je teoretično vsak 300-ti odvzem pozitiven. V praksi je velik odstotek krvodajalcev, ki ponovno pridejo dati kri in je tako tveganje manjše.

Test na protitelesa HC in tudi drugi testi, ki vključujejo ugotavljanje protiteles niso izpolnili vseh pričakovanj. Tvorba protiteles je plod reakcije organizma na tujek, ki pa je odvisna od vrste tujka in reaktivnosti organizma. V kolikor upoštevamo še občutljivost testa lahko ugotovimo, da so rezultati pogosto pozni. V zadnjem času zato uvajamo teste s katerimi lahko ugotovimo prisotnost posameznih molekul oziroma značilnih sekvenc molekul povzročiteljev. Ugotavljamo lahko prisotnost posameznih antigenov – povzročiteljev direktno in tako bistveno zmanjšamo diagnostično okno, saj smo izključili čas odgovora organizma in tvorbo protiteles. Novi testi so bistveno bolj občutljivi in tako primernejši za presejalno testiranje, obenem v pretežni meri odpravijo problem diagnostičnega okna.

## Virusi, ki jih lahko prenesemo s krvjo in krvnimi pripravki

Viruse, ki smo jih določili za "pomembne" pri prenosu bolezni s krvjo in krvnimi pripravki ( HIV, HB in HC), ugotavljamo v krvi ob vsakem odvzemu. Mnogi avtorji zagovarjajo tudi testiranje na prisotnost virusa HTLV-1( humani T limfocitni virus levkemije ). Značilnost vseh omenjenih virusov je, da povzročajo kronične bolezni, ki so za sedaj neozdravljive in to je verjetno glavni vzrok za njihovo pomembnost. Pri nekaterih pacientih sta pomembna tudi CMV ( cito megalo virus ) in parvovirus B19, ki se prenašata s krvjo, vendar smatramo okužbo iz okolja kot običajno, saj je okuženost v našem okolju pri CMV okoli 80% in zato klinično nista pomembna pri ljudeh z normalnim imunskim odgovorom. Podobno lahko v krvi zasledimo tudi Epstein Barr virus in nekatere viruse iz skupine herpes virusov, vendar v večini primerov klinično niso pomembni. Stopnja prekuženosti z virusom hepatitisa A je tudi zelo visoka in postane klinično pomemben ob izbruhu epidemij.

Rutinsko ugotavljanje vseh omenjenih virusov je mogoče, vendar v našem okolju ni praktično, saj bi ob visoki okuženosti izločili veliko večino potencialnih krvodajalcev obenem je prenos iz okolja prisoten v toliki meri, da eventuelna možnost prenosa s krvjo ni epidemiološko pomembna. Tveganje dejanskega prenosa pogostih virusov s krvjo in krvnimi pripravki je majhno, saj smo posamezniki v veliki večini že razvili protitelesa zaradi okužbe iz okolja. Problematični pa so lahko otroci, pacienti v izolaciji ali pacienti s pomankljivim imunskim odgovorom.

Tveganje prenosa okužb preko zdravil pripravljenih iz krvi je pogosto tako majhno, da potrebujemo matematične napovedne metode za oceno možnosti prenosa bolezni. Pri oceni stopnje tveganja posamezni testi za zaznavanje pokazateljev okužb pogosto odpovedo, saj niso zadosti občutljivi, zato uporabljamo metode za stopenjsko ugotavljanje možnosti prenosa virusov, ki jih na koncu seštejemo.

V Zahodni Evropi najpogosteje omenjajo, da lahko prenesejo HIV s krvjo v 1 od milijon odmerkov krvi. Pri nas glede na pojavnost in število okuženih posameznikov predvidevamo možen prenos na nekaj milijonov odmerkov ali drugače prikazano, teoretična verjetnost je en prenos infekcije HIV v 30 do 50 letih. V državah, kjer je pojavnost HIV-a večja, je tudi tveganje večje. Tudi v našem okolju se lahko spremeni, za sedaj ugodna epidemiološka situacija in se bomo v tem primeru približali evropski stopnji tveganja tj. možnosti prenosa HIVa v 10 letih. Ocenjena stopnja tveganja, ob uporabi klasičnih testov za ugotavljanje pokazateljev okužb, je pri hepatitisu B in C manjša od ena na 100 000, največkrat se omenja stopnja tveganja 1 na 200 000. Z uvajanjem testov na molekularni ravni pa se bo, po predvidevanjih, bistveno zmanjšalo tudi tveganje prenosa bolezni s transfuzijo krvi, seveda pa govorimo le o možnosti okužbe s pokazatelji, ki jih testiramo.

## Strokovno nejasni ukrepi

Prioni in z njimi povezana spongiformna encefalopatija so za sedaj za strokovno javnost še pretežno zaprta knjiga, ki pa jo iz dneva v dan bolje spoznavamo. Kljub temu, da ni strokovno jasnih dognanj, so že uvedeni določeni ukrepi. Vsakega krvodajalca sprašujemo po faktorjih tveganja in tako skušamo zmanjšati možnost prenosa bolezni. Filtriranje vse odvzete krvi je ukrep, ki nima strokovno dokazanega učinka na zmanjšanje prenosa prionov, ima pa številne pozitivne učinke, ki so posledica odstranitve levkocitov. S filtriranjem krvi zmanjšamo prenos CMV oziroma vseh možnih prenašalcev okužb, ki se nahajajo v levkocitih, zmanjšamo tudi stranske učinke levkocitov na imunski sistem in tudi učinke citokinov, ki se sproščajo po razpadu levkocitov. Odstranjevanje levkocitov s postopkom filtriranja krvi sigurno doprinese k varni transfuziji, ki pa ni strokovno dokazano pri prenosu prionov. Tudi ukrep dajanja

rekombinantnih faktorjev strjevanja krvi hemofilikom do 16. leta starosti, ki so ga uvedli v Angliji in Franciji, ima bolj političen priokus kot strokovno utemeljenost. Sežiganje vse plazme zbrane od krvodajalcev v Angliji si zelo težko strokovno razložimo, saj obenem filtrirane celične komponente krvi pridno uporabljajo. V nekaterih državah odklanjajo krvodajalce, ki so bivali v Angliji šest mesecev v obdobju od leta 1986. Ukrep je izsiljen, saj, če v Angliji sežigajo plazmo krvodajalcev potem jo tudi v drugih državah ne morejo uporabiti. Zakaj so določili rok šest mesecev pa ni možno strokovno utemeljiti, možne so le poljubne praktične razlage.

## Druge metode znižanja tveganja prenosa bolezni

Inaktivacija virusov v krvi je zelo obetavna možnost, ki navidezno postavlja pod vprašaj potrebnost predhodnega testiranja. Cilj inaktivacije virusov je, s praktičnega stališča, zmanjšati patogenost kužnih delcev na nivo, ki ni več kužen, in ohraniti molekule učinkovin ter celice čim bolj nedotaknjene. Metode inaktivacije virusov so zelo učinkovite pri posameznih pripravkih in obenem za razliko od metod testiranja delujejo nespecifično.

Za sedaj je uporaba metod inaktivacije in odstranjevanja virusov pri celičnih komponentah omejena vendar so metode zelo uspešne pri zdravilih pripravljenih iz krvi.

Ni opisanega primera prenosa virusov z albuminom, saj kot kaže, pasterizacija 10 ur na 60 °C odpravi tveganje.

Pri faktorjih strjevanja krvi so metode inaktivacije z detergenti in toplotno obdelavo sprejemljivo uspešne. Pri uporabi toplotnih tehnik moramo toplotno občutljive učinkovine zavarovati z dodajanjem aminokislin, sladkorjev ali citrata, vendar so izgube kljub temu vsaj 10 do 15%. Poleg zmanjšanja izkoristka lahko ob delovanju toplote na viruse pričakujemo tudi spremembe na učinkovinah oziroma poškodbo ali spremenjenost molekul beljakovin in posledično spremenjeno imunogenost oziroma slabšo učinkovitost.

Faktor IX lahko še dodatno filtriramo, saj je molekula zadosti majhna in ločljivost z nanofiltrom takšna, da odstranimo viruse .

Novejše tehnike inaktivacije posameznih pripravkov iz plazme, kot je inaktivacija z detergenti, nanofiltracija, toplotna obdelava, kemijsko učinkovanje s povečanjem kislosti v procesu priprave, delovanje alkohola ter kombinacije omenjenih metod, omogočajo dobro zaščito in močno zmanjšajo tveganje prenosa okužbe.

Tehnike inaktivacije se hitro spreminjajo in dopolnjujejo. Končni uporabniki praktično ne morejo slediti vsem novostim in jih kritično presojati, zato je pomembno sprotno spremljanje novosti in evaluacija novih tehnik. Pametna in sprotna izbira najboljših pripravkov lahko bistveno doprinese k varnosti.

Registracijski postopki in pregledi ter kontrolni mehanizmi ob uvozu ali dajanju zdravil v promet, ki delujejo administrativno, praviloma ne morejo hitro slediti vsem spremembam, vendar lahko bistveno prispevajo k povečani varnosti, predvsem s hitrimi ukrepi in ustaljenimi metodami izbire novejših ter varnejših pripravkov.

Pomemben element varnosti je nacionalni program samooskrbe, ki zajema enotno politiko oskrbe s plazemskimi proizvodi, pripravljenimi iz plazme zbrane v Sloveniji.

Novi rekombinantno pripravljeni nadomestki za pripravke humanega porekla so obetavni, saj se bomo z njihovo uporabo izognili prenosu večine sedaj aktualnih okužb. Vendar se okužbam in tveganju ne bomo mogli izogniti v celoti, saj bo možen prenos okužb vezanih na vrsto določenih celic, ki jih uporabljamo kot proizvajalke posameznega pripravka. Obenem še vedno uporabljamo za stabilizacijo rekombinantnih pripravkov substance humanega porekla in se zopet približamo tveganju, ki je vezano na pripravke humanega porekla.

Uporabnost pripravkov živalskega izvora je prav tako tvegana, saj se nam odpirajo nove možnosti prenosa bolezni značilnih za živalski svet. Pri zdravljenju hemofilikov s prisotnimi protitelesi lahko uporabimo faktor strjevanja krvi, ki je svinjskega porekla. Pomen in možnosti prenosa virusov ali drugih povzročiteljev bolezni od živali na človeka ni natančno določen, je pa verjeten.

Rekombinantno narejeni pripravki niso identični s pripravki humanega porekla in imajo pogosto nekoliko spremenjene molekule, obenem je njihovo fiziološko delovanje nekoliko drugačno. Za pripravo rekombinantnih pripravkov uporabljamo celice nehumanega porekla in lahko se razvijejo protitelesa na sicer podobne beljakovine, pripravljene z rekombinantno tehnologijo, ali na beljakovine nehumanega porekla, ki jih uporabljamo ob tehnološkem postopku.

## Dobra klinična praksa

Ugotovimo lahko, da idealno varnih pripravkov krvi ni, je pa stopnja varnosti tako velika, da jih lahko mirno uporabljamo v procesu zdravljenja. Najvišjo stopnjo varnosti dosežemo, če krvnih pripravkov ne uporabimo zato je ena od najpomembnejših nalog klinika, da natančno pretehta vse objektivne pokazatelje zdravstvenega stanja bolnika in ob uporabi znanja postavi indikacijo za transfuzijo krvi ali krvnih pripravkov. Pravilno postavljena indikacija bo tako najbolje pomagala bolniku do ohranitve življenja ali zboljšanja zdravlja.

Po postavljeni indikaciji, da moramo uporabiti kri in krvne pripravke v procesu zdravljenja, najprej pretehtamo možnost uporabe avtotransfuzije. Lastna kri je še vedno najbolj varna kri.

Analiza stranskih učinkov in napak v vseh državah in okoljih pokažejo, da je tri četrtine incidentov povezanih s tako imenovano administrativno napako oziroma napako v postopku. V vsakem okolju morajo izvajalci zdravstvenih storitev načrtovati take postopke, ki bodo izključili človeško zmotljivost ali jo znižali na minimum. Uporaba avtomatskih čitalcev za pozitivno identifikacijo prejemnika in enote krvi lahko bistveno pripomore k stopnji varnosti. V Sloveniji in tudi v drugih državah še ne moremo avtomatsko oziroma strojno identificirati posameznega prejemnika krvi, temveč to opravi zdravstveni delavec z vsemi možnimi tveganji, ki temeljijo na zmotljivosti posameznika. Vse naše znanje in tehnologija odpovedo ob zmoti glede identifikacije prejemnika zato moramo skrbno načrtovati postopke odvzema vzorcev krvi in dajanja transfuzije, ki morajo biti individualni.

Podobno moramo skrbno načrtovati vse nadaljne postopke, pošiljanja, sprejema, laboratoriske obdelave, izdaje izvida, prenosa krvi do prejemnika, in ponovne identifikacije prejemnika ter enote pripravka. Sam postopek dajanja pripravka moramo izvesti profesionalno z upoštevanjem standardnih predpisov.

Spremljanje pozitivnih in negativnih učinkov pa je končna stopnja v celotnem procesu zagotavljanja kakovosti, ki nam bo dala podatke za izboljšavo naših postopkov.

## Zaključek

Informiranost krvodajalcev in izobraževanje krvodajalcev, samoizključitev, konsultacija ter vodenje enotnega registra krvodajalcev, testiranje vsakega odmerka odvzete krvi, posebni postopki priprave komponent, določitev strogih indikacij za transfuzijo krvi in krvnih pripravkov, uporaba alternativnih metod zdravljenja, uporaba posebnih kirurških tehnik, uporaba tehnik avtotransfuzije, inaktivacija povzročiteljev okužb pri nekaterih pripravkih ter aktivna ali pasivna imunizacija so postopki, ki so bistveno znižali stopnjo tveganja prenosa bolezni s krvjo in njenimi pripravki.

Dober pregled in spremljanje informacij o procesu zbiranja krvi ali plazme, natančno spremljanje postopka predelave ali frakcionaže, skrbno izbrana kombinacija metod inaktivacije virusov, uporaba manjšega števila izbranih in varnih dajalcev ter kombinacija drugih medicinskih metod, kot so strokovna in načrtovana izbira pripravkov ob strogi indikaciji vezani za posameznega bolnika, uporaba alternativnih metod, uporaba administrativnih ukrepov, lahko zmanjšajo tveganje prenosa bolezni z zdravili pripravljenimi iz plazme na sprejemljivo raven, ob dobrih učinkih zdravljenja in sprejemljivi ceni.

Tveganje prenosa okužbe s krvjo in krvnimi pripravki je daleč nižje od tveganj, ki jih srečujemo v vsakdanjem življenju, zato lahko rečemo, da je transfuzija krvi in krvnih pripravkov varna.

Upoštevanje določil dobre klinične prakse pri uporabi krvi in krvnih pripravkov ter zdravil iz krvi lahko največ doprinesemo k znižanju stopnje tveganja in je najpomembnejši del celokupnega sistema zagotavljanja varnosti.

Vsak novi in dodatni postopek, ki doprinese svoj del varnosti, podraži končno učinkovitost. Vprašanje je, koliko denarja in energije smo pripravljeni nameniti določenemu znižanju tveganja, oziroma katera stopnja tveganja je sprejemljiva. Nabavna vrednost posameznih reagentov za vsakdanje testiranje krvi krvodajalcev stane praviloma nekaj mark do nekaj deset mark za en test. Upoštevaje stroške testiranja za 100 000 odvzemov, kolikor imamo krvodajalcev v Sloveniji letno, stane uvajanje dodatnega postopka nekaj milijonov mark na leto. Ob možnosti uvedbe nove metode moramo narediti tudi analizo finančne presoje, ki nam bo dala osnovo za ekonomske argumente uvedbe ali zavrnitve nove metode znižanja tveganja. Ob predhodni strokovni presoji mora finančna presoja zajeti vse stroške procesa zdravljenja, upoštevajoč stopnjo ozdravljenja ter stopnjo smrtnih posledic in stranskih negativnih učinkov, tako pri posameznem bolniku, kot tudi širše epidemiološke vplive.

V zadnjem času sprejemajo nekatere države bolj ali manj posrečene politične odločitve, Slovenija ni izločena iz dogajanja, ki pogosto nimajo trdnih strokovnih spoznanj, temveč govorijo o najboljši ali najbolj primerni rešitvi, saj zaradi pritiska javnosti ne morejo čakati na trdne strokovne izsledke in rešitve. Tako ob eventuelni finančni presoji uvajajo metode, ki naj bi imele pozitivne učinke z dobrim namenom zaščite prebivalcev. Od tu naprej je edini pogoj uvedbe nove metode, ki bo doprinesla k višji stopnji varnosti, finančna "zmožnost" odvisna od politične volje in strokovnih zmožnosti.

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# Tveganje in varnost pri navzkrižnem preizkusu

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## Uvod

Prve transfuzije krvi pred odkritjem krvnih skupin so se v velikem procentu neuspešno iztekle zaradi hemolitične transfuzijske reakcije. Odkritje krvnih skupin ABO pred 100 leti je omogočilo transfuzijo krvi, skladne v sistemu ABO. Hemolitične transfuzijske reakcije pa so se kljub temu prelomnemu odkritju še vedno dogajale. Kasneje so odkrili tudi številne druge krvne skupine, ki povzročajo imunizacijo in hemolitične transfuzijske reakcije (HTR). Uvajali so nove in vedno boljše metode laboratorijskih preiskav za ugotavljanje neskladnosti krvi pred transfuzijo. HTR bi morale danes izginiti iz seznama zapletov ob transfuziji krvi, vendar se to še ni zgodilo.

Prenos bolezni s krvjo je v zadnjih desetletjih 20. stol. na prvem mestu med nevarnostmi, ki se jih bolniki in zdravniki zavedajo in bojijo ob transfuziji krvi. Ob sistematičnem spremljanju neželenih učinkov transfuzije, ki lahko povzročijo smrt, so hemolitične transfuzijske reakcije na prvem mestu, ker transfuzija, neskladna v sistemu ABO, povzroči hemolitično transfuzijsko reakcijo, od blage, komaj prepoznavne, do takojšnje, hitro in dramatično potekajoče, s smrtnim izidom v najslabšem primeru. Do tega pride, ker imamo v krvi protitelesa anti-A in/oz. anti-B vedno, kadar na eritrocitih nimamo navedenih antigenov.

Položaj je enak po vsem svetu, kjer ta problem spremljajo (1,2,3,4).

Za preprečevanje teh zapletov imamo določene ukrepe v transfuzijskem laboratoriju in ob bolnikovi postelji. Obe področji sta tesno povezani in za varno transfuzijo ne zadošča izpopolnjen postopek le na enem; nujen je celovit sistem, ki zagotavlja varnost transfuzije tako pri delu v laboratoriju kot ob bolniku.

## Transfuziološke preiskave pred transfuzijo krvi

Trenutna doktrina predpisuje, da pred vsako transfuzijo opravimo določene preiskave. Te so naslednje:

1. Določitev krvne skupine ABO in RhD in eritrocitnih protiteles enote krvi za transfu-zijo se opravi takoj po odvzemu krvi. Vzorci so standardizirani in opremljeni s črtno kodo. Testiranje je mogoče avtomatizirati in celoten postopek voditi z računalniškim informacijskim sistemom. Na ta način se izognemo večini kritičnih postopkov, kjer lahko pride do človeške napake. Ob navzkrižnem preizkusu še zadnjikrat preverimo pravilnost določitve krvne skupine ABO in RhD enote krvi. Ob vseh teh postopkih je tveganje, da bi bila določitev napačna, izredno majhno.
2. Določitev krvne skupine ABO bolnika je osnovna in najpomembnejša preiskava, ker omogoči transfuzijo ABO skladne krvi.

   Zaradi izrednega pomena pravilne določitve krvne skupine ABO jo ob prvem določanju testiramo z dvema metodama, ob vsakem naročilu krvi za transfuzijo pa naredimo še kontrolno določitev, da izključimo event. možnost zamenjave krvnih vzorcev bolnikov.

   Metode določanja krvnih skupin so izpopolnjene, uporabljamo kakovostne testne serume in nove tehnike, tako da določitev krvne skupine v večini primerov ne predstavlja problema ob predpostavki, da testiramo pravilno odvzet vzorec krvi pravega pacienta.

Določanje krvne skupine ABO je oteženo v naslednjih primerih: krvi novorojenčkov s šibko izraženimi antigeni A in B, bolnikov z avtoimunsko hemolitično anemijo, agamaglobulinemijo, po zamenjavi krvne skupine ABO ob predhodni transfuziji, presaditvi kostnega mozga, malignih boleznih, infekcijah. V takih primerih so lahko motnje že pri orientacijskem določanju krvne skupine. Kadar je ob tem nujna transfuzija, tvegamo najmanj, če damo bolniku eritrocite krvne skupine O ali pa druge skladne krvne skupine.

3. Določitev antigena RhD je po pomembnosti na drugem mestu, kajti v krvi protitelesa anti-D normalno niso navzoča, vkolikor RhD-negativna oseba ni bila v stiku z RhD-pozitivnimi eritrociti, kar se lahko zgodi le ob transfuziji ali nosečnosti. V navedenem primeru pa človek v 80% tvori anti-D protitelesa, ki ob transfuziji RhD pozitivne krvi povzročijo hemolizo RhD-pozitivnih eritrocitov. Posebnost pri določanju antigena RhD je v tem, da ima mnogo ljudi šibko izražene antigene, sicer pa motijo določitev predvsem avtoimunska obolenja.
4. Določitev drugih antigenov sistema Rh(C,E,c,e) ali drugih krvnih skupin (K,k,Jka,Jkb,Fya,Fyb,MNSs in drugih) je nujna v primerih imunizacije po transfuziji ali nosečnosti.
5. Navzkrižni preizkus naredimo potem, ko smo določili krvno skupino in izbrali za transfuzijo kri enake oz. skladne krvne skupine ABO in RhD, kot jo ima bolnik.

   Z navzkrižnim preizkusom v najprej preverimo pravilnost določitve krvne skupine ABO in RhD bolnika-prejemnika in dajalca, nato pa pomešamo kri prejemnika in dajalca in v laboratorijskih pogojih naredimo to, kar se ob transfuziji dogaja v obtočilih prejemnika krvi. S tem testom ugotavljamo protitelesa v krvi prejemnika, ki bi povzročila hemolizo transfundiranih eritrocitov. Po navedbi iz literature ima taka protitelesa približno 1% vseh bolnikov, pri katerih naredimo presejalni test (5). Za testiranje uporabljamo serološke metode, s katerimi odkrijemo čim več klinično pomembnih protiteles. Ob tem je pomembna občutljivost testa; biti mora tako velika, da ugotavljamo vsa pomembna protitelesa, ne želimo pa tako velike, da bi ugotavljali protitelesa, ki za preživetje eritrocitov niso pomembna. V takem primeru bi morali raziskovati njihovo specifičnost, ki za preživetje transfundiranih eritrocitov ni pomembna, bi pa to lahko predstavljalo povečano tveganje za prejemnika, ker krvi ne bi dobil o pravem času.

## Tveganje za nastanek HTR pri politransfundiranih bolnikih

Pri bolnikih, ki so dobili transfuzijo krvi v bližnji ali daljni preteklosti, je tveganje za HTR večje kot pri tistih, ki transfuzije niso še nikoli dobili. Za nobeno transfuzijo namreč ne moremo pripraviti eritrocitov, skladnih med prejemnikom in dajalcem v vseh eritrocitnih antigenih, zato vedno obstoji tveganje imunizacije. Če protitelesa nastanejo, je vprašanje, ali so ob času testiranja pred transfuzijo prisotna v zadostni količini, da jih odkrijemo z rutinskimi preiskavami. Za te bolnike je posebno pomembno, da so nam dostopni podatki o preteklih preiskavah, kajti za take bolnike lahko izberemo skladno kri le na podlagi take informacije (6).

Lahko pa se zgodi, da se je količina teh protitelesa zmanjšala pod mejo dokazljivosti. V takem primeru bo verjetno prišlo do odložene HTR, ki je ni bilo mogoče preprečiti. To je neizogibno transfuzijsko tveganje.

Nadaljna neugodna možnost je, da se poleg že diagnosticiranih protiteles pojavijo dodatna protitelesa, ki jih ob prejšnjem testiranju še ni bilo.

Eritrocitna protitelesa pa nastanejo tudi med in/ali po nosečnosti, zato so pomembni tudi podatki o nosečnostih, porodih in splavih, prav tako kot o transfuzijah.

Včasih je podatke o nosečnostih in transfuzijah težko dobiti zaradi bolnikovega kliničnega stanja, ali je na dogodek pozabil ali pa iz osebnih razlogov o njem ne želi govoriti.

## Avtoimunska obolenja in transfuzija

Pri bolnikih z avtoimunsko hemolitično anemijo s toplimi protitelesi ni mogoče pripraviti krvi z negativnim navzkrižnim preizkusom, ker njihova avtoprotitelesa reagirajo z vsemi eritrociti. Kadar tak bolnik nujno potrebuje kri, mu moramo dati eritrocite s pozitivnim navzkrižnim preizkusom. Za tako transfuzijo se odločimo po dogovoru z lečečim zdravnikom le takrat, ko je bolnik zaradi hude anemije življenjsko ogrožen in alternativno zdravljenje ne zadostuje. V takem primeru moramo vedno poskusiti ugotoviti, ali ima bolnik poleg avtoprotiteles event. prisotna aloprotitelesa, ki so lahko nastala po pretekli transfuziji ali nosečnosti. Pogostost takih protiteles je po navedbah v literaturi 15 do preko 40% (7). Kadar so taka protitelesa prisotna, moramo izbrati eritrocite brez antigena, proti kateremu so uperjena protitelesa. Pri bolnikih, ki takega dogodka nimajo v anamnezi, se laže odločimo za transfuzijo kljub pozitivnim rezultatom navzkrižnega preizkusa. Preživetje transfundiranih eritrocitov je pri takih bolikih približno enako skrajšano kot njihovih lastnih eritrocitov.

## Transfuzija krvi v nujnih primerih

Zdravnik, ki naroči transfuzijo krvi brez zaključenega navzkrižnega preizkusa, se mora zavedati, kakšno je tveganje hemolitične transfuzijske reakcije. Pri transfuziji krvi krvne skupine O,RhD-negativne brez navzkrižnega preizkusa ni tveganja hemolize zaradi anti-A in anti-B protiteles, lahko pa so pri bolniku prisotna protitelesa proti antigenom drugih krvnih skupin, ki povzročajo hemolizo eritrocitov (4,8).

Ob transfuziji krvi iste krvne skupine, kot jo ima bolnik in brez navzkrižnega preizkusa, je tveganje večje kot v prejšnjem primeru, ker lahko pride do napake ob identifikaciji bolnika, odvzemu vzorca krvi ali v laboratoriju in kot posledica te napake do neskladnosti transfuzije v sistemu ABO.

Ob transfuziji krvi v nujnem primeru moramo upoštevati vsa navodila za delo enako kot pri planiranih transfuzijah. Poleg tveganja neželjenih učinkov transfuzije, ki se jim ne moremo popolnoma izgniti, je večja možnost napak pri vseh postopkih, ker zaradi nujnosti primera hitimo in imamo večje število nujnih opravil naenkrat (tab. 1).

**Tabela 1. Naročanje krvi in testiranje v nujnih primerih**

| Stopnja nujnosti | Krvna skupina krvi za transfuzijo | Opombe in priporočila |
|---|---|---|
| Nujna takojšnja transfuzija | O,RhD negativna<br>Brez NP | 0,2-0,6% populacije ima eritrocitna protitelesa(8), huda hemoliza ni pogosta. Kadar to ne ogroža bolnikovega življenja, počakati na kri iste krvne skupine. |
| 15 min.po prejemu vzorca<br>I.faza po telefonu | Kri iste ali skladne krvne skupine.<br>Kontrola ABO/RhD prejemnika in krvi.<br>Brez NP | Počakati na zaključek NP, če to ne pomeni pomembnega tveganja za bolnika. |
| 45 min. po prejemu vzorca<br>I. faza | Kri iste ali skladne krvne skupine.<br>Zaključen NP | Vzorec bolnikove krvi ima prednost pri testiranju.<br>V primeru prsotnosti prititeles dodatno testiranje in posvet. |

*NP: navzkrižni preizkus*

## Informacijski sistem v transfuzijskem laboratoriju

Za varnost transfuzije je velikega pomena pregled in primerjava podatkov o transfuzijskih preiskavah bolnikove krvi v preteklosti in sedanjega naročila in rezultatov testiranja; v primerih njihove neskladnosti ali kakršnihkoli pozitivnih rezultatov, motenj ali neželjenih učinkov transfuzije krvi v preteklosti pa posredovanje opozorila.

Kadar je prenos informacij odvisen le od upoštevanja navodil za delo, organizacije dela in človeškega spomina, je vedno v nevarnosti, da odpove, zato je za zmanjšanje tveganja neskladne transfuzije izredno pomembna uporaba računalniškega informacijskega sistema, ki nam tak pregled podatkov omogoča.

Računalniški informacijski sistem omogoča učinkovit prenos za transfuzijo pomembnih informacij v transfuzijski ustanovi ter zmanjša tveganje človeške napake od odvzema enote krvi do njene izdaje na bolnišnični oddelek (9, 10).

Za varno transfuzijo je po pomembnosti na prvem mestu informacija o določitvi prejemnikove krvne skupine ABO v preteklosti, ki jo primerjamo z novim rezultatom. Dvakratna določitev iste krvne skupine pri bolniku je dovolj dobro zagotovilo, da ni bilo napake ne ob odvzemu vzorca krvi in ne ob laboratorijskem testiranju ali administrativnih postopkih. V primeru kakršnekoli neskladnosti teh podatkov moramo razjasniti primer, preden bolnik dobi transfuzijo. Pomembno pa je, da za neskladnost določitev krvnih skupin vemo. V primeru ročnega prepisovanja podatkov se lahko zgodi, da je nihče ne opazi ali ne poišče starega rezultata, če pa so podatki vpisani v računalniško bazo podatkov, nas računalnik opozori na neskladnost in nam ne dovoli nadaljevati dela, dokler ne razrešimo nejasnosti.

Prenos informacij o pozitivnih rezultatih testiranja v preteklosti je velikega pomena tudi za preprečevanje odložene hemolitične transfuzijske reakcije pri bolnikih z nizkimi titri eritrocitnih protiteles. Običajno so ti podatki shranjeni na različnih mestih v laboratorijih in v bolnišnicah, lahko jih dobimo od bolnika samega ali njegovega zdravnika ali pa iz kartoteke senzibiliziranih paciemtov, toda iz prakse vemo, da je tako opozorilo le redko posredovano (10). Ob uporabi računalniškega informacijskega sistema pa se v primeru pozitivnega izsledka iz preteklosti ob vnosu novega naročila za kri na ekranu pojavi opozorilo in se izpiše tudi na delovni nalog za laboratorij. Na osnovi teh sporočil lahko izdamo izvid in kri za transfuzijo le, če so eritrociti brez antigenov, proti katerim so usmerjena protitelesa.

V bazi podatkov so poleg podatkov o rezultatih laboratorijskih preiskav shranjeni tudi komentarji in medicinske opombe za bolnike. Med njimi so posebno pomembni podatki o zapletih ob transfuzijah, zlasti o neželenih stranskih učinkih transfuzije, s transfuzijskimi reakcijami (hemolitičnimi, anafilaktičnimi, alergičnimi in drugimi) na prvem mestu. Medicinske opombe, n.pr. o zamenjavah krvne skupine ob prejšnji transfuziji, presaditvi kostnega mozga itd. se zbirajo v podatkovni bazi na osnovi rezultatov laboratorijskih preiskav ali pa po odločitvi zdravnika in so lahko zelo pomembne pri nadaljni strokovni obravnavi bolnika.

Teh podatkov pa seveda ni, če ne dobimo sporočila o neželenem učinku transfuzije od zdravnika, ki bolnika zdravi. To je razlog, da imamo v novem Zakonu o preskrbi s krvjo(11) zapisan 36. člen, ki predpisuje lečečemu zdravniku poročanje o neželenih učinkih transfuzije.

## Zaključek

Z uporabo sodobnih metod za zagotavljanje transfuzije skladne krvi zmanjšamo tveganje za hemolitično transfuzijsko reakcijo tako pri tistih, ki bodo prvč dobili transfuzijo krvi kot pri politransfundiranih bolnikih, pri avtoimunskih obolenjih in transfuzijah v nujnih primerih. Varnost transfuzije poveča tudi uporaba računalniškega informacijskega sistema v transfuzijskem laboratoriju. Tveganje za neskladno transfuzijo bo še zmanjšalo spremljanje učinkov transfuzije in uvedba celovitega informacijskega sistema tudi na bolnišnične oddelke. Čim manjša bo možnost človeške napake, manjše bo tveganje za neskladno transfuzijo. Zavedati pa se moramo, da sto procentne varnosti ni mogoče doseči. To neizogibno transfuzijsko tveganje je eden od razlogov za racionalno zdravljenje s krvjo.

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# Pregled predpisov, ki urejajo področje prometa s krvjo in zdravil iz krvi

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## Izvleček:

Z uveljavitvijo Evropskega pridružitvenega sporazuma je Republika Slovenija postala pridružena država Evropske unije in se obvezala, da bo svoj pravni red uskladila z evropskim pravnim redom.

Vlada Republike Slovenije je sprejela Državni program za prevzem Evropskega pravnega reda, v katerem je opredelila časovno dinamiko za sprejem posameznih pravnih aktov.

Področje zdravil in medicinskih pripomočkov sodi med najbolje regulirana področja. Vendar znanstveno tehnični razvoj vpliva tudi na razvoj zakonodaje o zdravilih in terja nenehne spremembe in dopolnitve, ki jim mora regulatorni organ z vidika cilja varovanja javnega zdravja dosledno slediti.

Zakonodaja s področja zdravil je tako kot vsa ostala zakonodaja Republike Slovenije v zadnjem času doživela veliko preobrazbo.

Z uveljavitvijo Evropskega pridružitvenega sporazuma je Republika Slovenija 1. februarja 1999 postala pridružena država Evropske unije. Evropski pridružitveni sporazum je mednarodna pogodba, ki je v skladu z Ustavo Republike Slovenije postal del njenega pravnega reda. Pravno ureditev Republike Slovenije delno nadgrajuje, delno pa ureja področja, ki v domači zakonodaji niso še urejena.

S prevzemom Evropskega pridružitvenega sporazuma smo prevzeli obvezo, da bomo slovenski pravni red uskladili z acquis communautaire, to je z Evropskim pravnim redom. Skupna zakonodaja držav članic je namreč pomembno sredstvo integracije Evropske unije, poenotenje zakonodaje pa je eden od načinov za doseganje ciljev Evropske skupnosti.

Zato je harmonizacija zakonodajnega področja logična in nujna posledica naše odločitve. Časovno dinamiko sprejemanja harmonizirane zakonodaje je Republika Slovenija določila z Državnim programom za prevzem Evropskega pravnega reda.

Vlada Republike Slovenije je sprejela v začetku leta 1999 zelo ambiciozen program, po katerem naj bi Državni zbor v tem letu sprejel okrog 80 zakonskih projektov in do konca leta 2000 vrsto podzakonskih aktov, ki bodo urejali posamezna področja. V programu sta bila za leto 1999 določena tudi **Zakon o zdravilih in medicinskih pripomočkih** (Uradni list RS, št. 101/99 in 70/00) in Zakon o preskrbi s krvjo. Oba zakona sodita v področje zdravil, ki je eno najbolje reguliranih področij, kajti bistveni cilj vseh predpisov, ki urejajo proizvodnjo, distribucijo ali uporabo zdravil, je zagotavljanje visoke stopnje zaščite javnega zdravja.

Pomembna določila, ki jih glede na specifično naravo zdravil in na prednostni vidik zdravja prebivalstva predstavlja Evropska unija so zagotovila, da:

- zakonodajni organ jamči, da zdravila ustrezajo znanstvenim merilom glede kakovosti, varnosti in učinkovitosti predno so dana v promet,
- nacionalni pristojni organi za zdravila izdajajo dovoljenja za promet z zdravilom, ki temeljijo na merilih in standardih Evropske skupnosti,
- so pogoji po katerih so zdravila izdelana na visoki kakovostni ravni in da ustrezajo pravilom Dobre proizvodne prakse,

- so izdana dovoljenja za proizvodnjo zdravil na osnovi inšpekcijskih pregledov,
- so predpisi za trženje, grosistična distribucija, klasifikacija, označevanje zdravil in oglaševanje usklajeni z direktivami Evropske unije.

Z ozirom na definicijo osnovne direktive Sveta 65/65/EEC glede uskladitve določil, vsebovanih v zakonih, predpisih in upravnih postopkih, ki veljajo za zdravila, štejejo med zdravila tudi človeška kri, krvni pripravki in krvni izdelki, čeravno poglavje II. do V. te direktive ne veljajo za nekatera zdravila, med katera štejejo kri, plazma in pripravki iz krvnih celic človeškega izvora.

Krvne izdelke, ki vsebujejo albumine, faktorje koagulacije in imunoglobuline in so izdelani iz človeške ali živalske krvi s farmacevtskimi in kemičnimi metodami pa šteje med zdravila, za katera veljajo določbe direktive Sveta 65/65/EEC in 75/319/EEC s spremembami in dopolnitvami ter vse direktive sveta, ki natančneje določajo posamezna poglavja.

Harmonizacija zakonodaje področja, ki obsega kri, krvne pripravke in krvne izdelke je tako narekovala pripravo dveh zakonskih predpisov od katerih pokriva Zakon o preskrbi s krvjo kri in krvne pripravke, Zakon o zdravilih in medicinskih pripomočkih pa pokriva krvne izdelke. Načelo nacionalne samozadostnosti za varno preskrbljenost prebivalstva z vsemi oblikami zdravil iz krvi in krvne plazme ureja Zakon o preskrbi s krvjo, dopolnjujejo pa ga izvršilni predpisi, izdani na podlagi Zakona o zdravilih in medicinskih pripomočkih.

V svojem pregledu se bom omejila na predpise, ki se nanašajo na zdravila le v delu, ki se nanaša na krvne izdelke.

Z Zakonom o zdravilih in medicinskih pripomočkih (Uradni list RS, št. 101/ 16. 12. 1999 in 70/00) so v kontekstu usklajenih javno zdravstvenih pravil upoštevane horizontalne direktive Sveta Evrope, ki se uvrščajo med UKREPE I. stopnje, s katerimi je zagotovljen celovit okvir za podrobnejšo zakonodajo. Nanašajo se na:

- razvrščanje zdravil,
- dovoljenje za promet z zdravili,
- preskušanje zdravil,
- dovoljenje za izdelavo zdravil,
- promet z zdravili,
- označevanje in oglaševanje zdravil,
- kontrolo kakovosti zdravil ter
- nadzor nad izvajanjem zakona in predpisov izdanih na njegovi podlagi.

V vseh teh temeljnih poglavjih so zajeta tudi določila, ki se nanašajo na krvne izdelke.

Način razvrščanja zdravil, predpisovanja in izdajanja zdravil opredeljuje **PRAVILNIK o natančnejši opredelitvi, načinu razvrščanja, predpisovanja in izdajanja zdravil za uporabo v humani medicini** (Uradni list RS, št. 37/5. 5. 2000)

Krvni izdelki so lahko v prometu le, če je bilo zanje izdano dovoljenje za promet in pod pogoji, ki jih določa 9. člen Zakona o zdravilih in medicinskih pripomočkih.

Z zakonom je predpisana tudi veljavnost Evropske farmakopeje. Veljavnost dodatkov in sprememb k Evropski farmakopeji je objavljena tekoče v Uradnem listu RS.

**SKLEP o uveljavitvi sprememb in dopolnitev tretje izdaje Evropske farmakopeje** (Uradni list RS, št. 7/28.1.2000)

**SKLEP o veljavnosti četrtega dodatka k tretji izdaji Evropske farmakopeje** (Uradni list RS, št. 101/6. 11. 2000)

**PRAVILNIK o postopku pridobitev dovoljenja za promet z zdravilom** (Uradni list RS, št. 67/28. 7. 2000), ki določa:

- vsebino predloga, postopek in pogoje za pridobitev dovoljenja za promet z zdravilom
- obliko zahtevane dokumentacije
- navedbo pogodbenih firm, ki so bile udeležene pri proizvodnji ali pri validaciji krvnih izdelkov
- postopek in vsebino dokumentacije, potrebne za obnovo dovoljenja za promet
- postopek za spremembo dokumentacije, oziroma dovoljenja za promet
- prenehanje veljavnosti dovoljenja za promet
- postopek za prenos dovoljenja za promet.

Področje krvnih izdelkov pokriva tudi:

**ODREDBA o določitvi enotnega nacionalnega poimenovanja zdravilnih učinkovin in sistemu razvrščanja zdravil po anatomsko-terapevtsko kemični klasifikaciji** (Uradni list RS, št.72/11. 8. 2000)

Preskušanje zdravil je določeno z zakonom. Preden je zdravilo dano v promet mora biti:

- analizno
- farmakološko toksikološko
- klinično preskušeno

Pogoji, ki jih morajo izpolnjevati preskuševalci za analizno preskušanje zdravil so določeni s **PRAVILNIKOM o pogojih, ki jih morajo izpolnjevati preskuševalci za analizno preskušanje zdravil in postopek njihovega preverjanja** (Uradni list RS, št. 43/24. 5. 2000).

Sama določila o analiznem preskušanju, podrobnejša vsebina in struktura farmacevtsko-kemičnega, biološkega in mikrobiološkega dela dokumentacije so določena s **PRAVILNIKOM o analiznem preskušanju zdravil** (Uradni list RS, št. 73/19. 8. 2000).

Pomembno določilo tega pravilnika v zvezi s krvnimi izdelki je navedeno v poglavju kontrola kakovosti vhodnih snovi - 24. člen, ki navaja, da je potrebno pri izdelkih, pridobljenih iz človeške krvi ali plazme opisati in dokumentirati izvor ter merila in postopke za zbiranje, prevoz in shranjevanje izvornega materiala. Uporabiti se sme samo opisane in definirane zbire izvornega materiala. Opis vhodne snovi mora zajemati strategijo izdelave, postopke prečiščevanja/inaktivacije, ki morajo biti validirani ter vse postopke medfazne kontrole, namenjene za zagotavljanje kakovosti in varnosti ter konsistentnosti serij, zlasti glede prenosa virusnih in drugih bolezni, ki se prenašajo s krvjo in prenosa transitorne spongiformne encefalopatije (TSE).

Način farmakološko-toksikološkega preskušanja zdravila in vsebino farmakološko-toksikološkega dela dokumentacije, ki je sestavni del predloga dovoljenja za promet z zdravilom določa **PRAVILNIK o farmakološko-toksikološkem preskušanju zdra**vil (Uradni list RS, št. 44/26. 5. 2000).

**PRAVILNIK o kliničnem preskušanju zdravil** (Uradni list RS, št. 67/28. 7. 2000) določa sam postopek, vsebino dokumentacije za odobritev ali priglasitev kliničnega preskušanja zdravila, pravice in dolžnosti udeležencev v preskušanju, pristojnosti Urada Republike Slovenije za zdravila in vsebino kliničnega dela dokumentacije za pridobitev dovoljenja za promet z zdravilom.

Med temeljne določbe zakonodaje s področja zdravil, katerih cilj je zaščita javnega zdravja po evropskih standardih in obenem zagotovitev prostega pretoka blaga ter preprečevanje uvoza oporečnih zdravil, sodita poglavji o izdelavi in prometu z zdravili.

Zdravila se lahko izdelujejo le na podlagi dovoljenja za izdelavo zdravil, ki ga izda Urad Republike Slovenije za zdravila.

Okvirne pogoje določa zakon, natančnejše pogoje, ki jih morajo izpolnjevati izdelovalci zdravil, postopek ugotavljanja pogojev, postopek izdajanja in odvzema potrdila o izvajanju dobre proizvodne prakse pa določa **PRAVILNIK o natančnejših pogojih, ki jih morajo izpolnjevati pravne ali fizične osebe za pridobitev dovoljenja za izdelavo zdravil, postopek ugotavljanja pogojev in postopek izdajanja in odvzema potrdila o izvajanju dobre proizvodne prakse** (Uradni list RS, št. 94/13. 10. 2000).

Dodatni pogoji za izdelavo zdravil, ki sodijo med krvne izdelke pa opredeljuje **PRAVILNIK o zdravilih, ki so pridobljena iz človeške krvi ali plazme**, ki je v vladni proceduri.

Isti pravilnik določa tudi dodatne pogoje za promet s krvnimi izdelki, ki niso vsebovani v določbah zakona, ki se nanašajo na promet z zdravili in v **PRAVILNIKU o natančnejših pogojih za promet na debelo z zdravili iz skupin A, B in C ter postopek verifikacije in preverjanja** (Uradni list RS, št. 2/15. 1. 1999).

Pri prometu s krvnimi izdelki se upošteva načelo samozadostnosti, ki ga podpira Svet Evrope in je vsebovano v Zakonu o preskrbi s krvjo. Posebej pa je določeno, da v izjemnih primerih na predlog klinike ali inštituta Urad Republike Slovenije za zdravila dovoli uvoz tudi krvnega izdelka, ki nima dovoljenja za promet v Republiki Sloveniji.

Uvoz zdravil, ki imajo dovoljenje za promet v Republiki Sloveniji je prost. Ne glede na to, pa je pri vsakokratnem uvozu krvnih izdelkov potrebno posebno dovoljenje Urada Republike Slovenije za zdravila. Postopek za pridobitev posebnega dovoljenja za uvoz krvnih izdelkov je določen s **PRAVILNIKOM o pogojih in postopku za pridobitev posebnega dovoljenja za uvoz zdravil in medicinskih pripomočkov** (Uradni list RS, št. 72/11. 8. 2000).

V drugem poglavju, se izrecno zahteva zagotovilo, da izdelek ne vsebuje oziroma ne izvira iz specifičnega rizičnega materiala glede prenosljive spongiformne encefalopatije (TSE).

Označevanje krvnih izdelkov je določeno s **PRAVILNIKOM o označevanju zdravil in o navodilu za uporabo** (Uradni list RS, št. 82/20. 9. 2000) v katerem poleg ostalih določb obravnavata kri in krvne izdelke - člena 10. in 11.

**PRAVILNIK o farmakovigilanci** (Uradni list RS, št 94/13. 10. 2000) določa način spremljanja neželenih škodljivih učinkov zdravil, pogoje, ki jih mora izpolnjevati pravna oseba, ki je določena za to dejavnost s strani ministra ter obveznosti udeležencev v sistemu farmakovigilance. Ta pravna oseba je dolžna spremljati tudi neželene škodljive učinke medicinskih pripomočkov po zakonu in pravilniku, ki ureja to področje in kamor sodijo tudi izdelki, ki se uporabljajo pri transfuzijski in kirurški dejavnosti. Pravna oseba za spremljanje škodljivih učinkov zdravil in medicinskih pripomočkov je bila imenovana z: **ODREDBO o določitvi pravne osebe za spremljanje neželenih škodljivih učinkov zdravil in neželenih škodljivih učinkov medicinskih pripomočkov** (Uradni list RS, št. 100/27. 10. 2000).

Glede obveščanja o zdravilih in oglaševanja zdravil veljajo za krvne izdelke določbe zakona in **PRAVILNIKA o oglaševanju zdravil in medicinskih pripomočkov** (Uradni list RS, št. 59/97).

Kontrolo kakovosti krvnih izdelkov obravnava zakon, ki v 73. členu določa posebno kontrolo kakovosti vsake serije rizičnih zdravil, med katera sodijo tudi krvni izdelki.

Poglavje Zakona o zdravilih in medicinskih pripomočkih, ki se nanaša na medicinske pripomočke sega tudi na področje krvnih izdelkov.

**PRAVILNIK o medicinskih pripomočkih** (Uradni list RS, št. 82/20. 9. 2000) natančno določa pogoje za izdelavo medicinskih pripomočkov, bistvene zahteve pogoje ugotavljanja skladnosti, način razvrščanja, pogoje za dobavitelje in pogoje priglasitve ter pogoje kliničnega preskušanja medicinskih pripomočkov.

Med medicinske pripomočke sodijo s področja transfuzijske dejavnosti na primer ves pribor iz medicinske plastike za enkratno uporabo, igle, brizge, reagenti in na primer vrečke za kri, ki sodijo v razred II. b in III., kar pomeni visoko stopnjo tveganja za uporabnika.

Za področje zdravil in medicinskih pripomočkov sta bili izdani tudi dve Odredbi o stroških postopkov, ki jih izvaja po zakonu Urad Republike Slovenije za zdravila. To sta:

**ODREDBA o stroških** (Uradni list RS, št. 93/12. 10. 2000)

**ODREDBA o spremembah in dopolnitvah odredbe o stroških** (Uradni list RS, št. 109/ 28. 11. 2000).

Predstavljena zakonodaja, v kateri so obravnavana zdravila in med njimi krvni izdelki je v celoti harmonizirana z Evropskim pravnim redom. Implementacija predpisov se izvaja od uveljavitve Zakona o zdravilih in medicinskih pripomočkih, od 1. 1. 2000.

Urad Republike Slovenije za zdravila je izpolnil obveze iz Državnega program za sprejem Evropskega pravnega reda v celoti.

Kot je bilo že uvodoma poudarjeno, sodi področje zdravil med najbolje regulirana področja. Znanstveno tehnični razvoj pa odpira tudi na področju zdravil nova vprašanja in dileme, zaradi česar je dopolnjevanje predpisov spremljajoče delo. V Evropski uniji se pripravljajo spremembe in dopolnitve zakonodaje o zdravilih v projektu Revizija 2001.

V skupini EMACOLEX, ki jo sestavljajo strokovnjaki in pravniki, aktivno sodeluje tudi Urad Republike Slovenije za zdravila.

# Hemovigilanca
# Haemovigilance

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## Izvleček

Hemovigilanca je nacionalni sistem nadzorovanja in opozarjanja celotne transfuzijske dejavnosti od izbire krvodajalcev do spremljanja prejemnikov krvnih pripravkov, ki zbira in analizira vse neželene učinke transfuzije s ciljem, da bi odklonili vzroke njihovega nastanka in preprečili njihovo ponovno pojavljanje. V državah z ustanovljenim sistemom hemovigilace, je slednja postala temeljni kazalec kakovosti transfuzijske službe. V Sloveniji smo hemovigilanco predpisali z zakonom, prijavljanje neželenih učinkov pa je zakonska obveza. Sistem hemovigilance bomo v celoti zgradili v bližnji prihodnosti.

Ključne besede: *hemovigilanca, transfuzija, neželeni učinki, komponente krvi.*

## Abstract

Haemovigilance is a national system of surveillance and alarm in transfusion activities from blood donor selection to the follow-up of the blood component recipients, gathering and analysing all untoward effects of blood transfusion in order to correct their cause and prevent recurrence. In countries where haemovigilance has been established, it became the ultimate quality indicator of a transfusion service. In Slovenia haemovigilance was created by law and notification of transfusion incidents is a legal obligation. But the whole system of haemovigilance will be established in the near future.

Key words: *haemovigilance, blood transfusion, untoward effects, blood components.*

## Uvod

Varnost transfuzije je postala paradigma v transfuzijski medicini na začetku osemdesetih let kot odziv na pojav in posledice prenosa okužb z virusom HIV s transfuzijami krvnih pripravkov. V tem času so medicinski strokovnjaki in zdravstvene oblasti sprožili številne strokovne, organizacijske in tudi konceptualne posege v sistem preskrbe s krvjo in krvnimi pripravki z namenom izboljšanja njihove varnosti. V transfuzijsko dejavnost so, po vzoru na farmakovigilanco, uvedli tudi hemovigilanco, ki je v začetku pomenila sistematičen nadzor nad neželenimi učinki po transfuziji krvnih pripravkov. Pozneje so njen obseg preširili in dopolnili, tako da danes pod pojmom hemovigilanca razumemo sistem organiziranega nadzora transfuzijske dejavnosti od zbiranja krvi in krvnih pripravkov do njihove transfuzije bolnikom z namenom zaznavanja, spremljanja, vodenja in vrednotenja informacij o neželenih učinkih transfuzije ter zato, da bi odklonili vzroke njihovega nastanka in preprečili ali zmanjšali njihovo ponovno pojavljanje (1). Naziv hemovigilanca so prvič uvedli v Franciji leta 1993 (2). Kmalu za tem so koncept hemovigilance sprejele tudi številne druge države. Odbor ministrov Sveta Evrope v 6. izdaji Dodatka k Priporočilu št.R (95) 15 o pripravi, uporabi in zagotavljanju kakovosti komponent krvi, obravnava hemovigilanco kot del sistema zagotavljanja kakovosti v transfuzijski dejavnosti in jo skupaj s farmakovigilanco in materiovigilanco uvršča v sistem zdravstvenovarnostnega nadzora v državi (3).

## Cilj hemovigilance

Glavni cilj hemovigilance je kar najbolj varna, racionalna in učinkovita transfuzija krvnih pripravkov. Poskušamo ga doseči s prospektivnim nadzorom nad neželnimi učinki celotnega transfuzijskega procesa in ukrepi za njihovo preprečevanje ter s pravočasnim opozarjanjem na njihovo pojavljanje.

Dodatni cilj hemovigilance je povečanje zaupanja v sistem preskrbe s krvjo. Hemovigilanca je zanesljiv vir, ki zagotavlja in posreduje zdravstvenim strokovnjakom in oblastem ter širši javnosti objektivne informacije o neželenih učinkih transfuzije, kar omogoča oblikovanje objektivnega mnenja o varnosti in tveganjih transfuzije ter tako povečuje zaupanje v sistem preskrbe s krvjo (4).

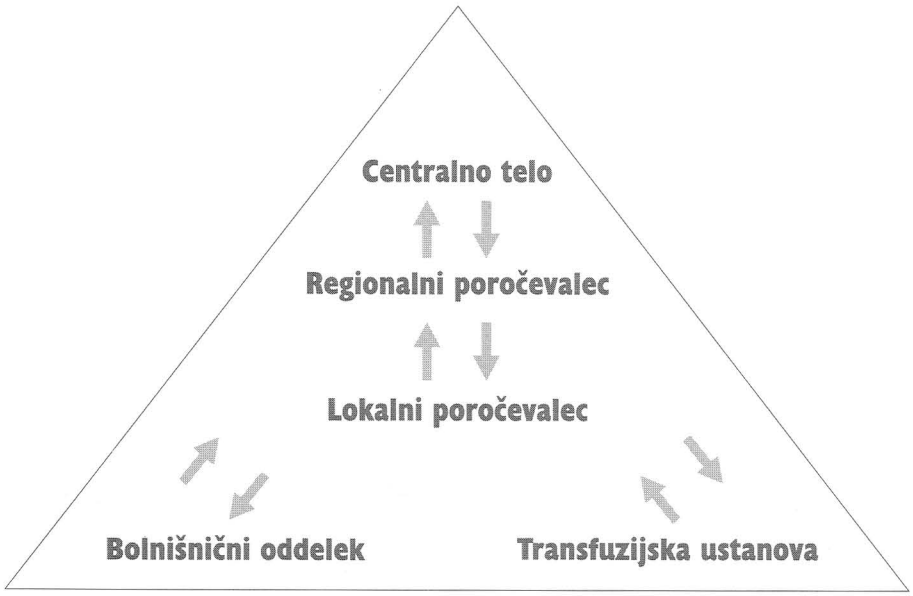
## Organizacija hemovigilance

Organizacija hemovigilance je večinoma prilagojena potrebam in značilnostim preskrbe s krvjo in zdravstvenega varstva v posamezni državi. Poznamo več načinov organiziranosti hemovigilance. V državah, kjer so reorganizirali in centralizirali transfuzijsko službo, so praviloma zasnovali tudi enoten in samostojen sistem hemovigilance (Francija, Velika Britanija, Nizozemska) (5). Drugje pa so hemovigilanco priključili k sistemu farmakovigilance (Švica) (5). Hemovigilanca v ZDA je sestavljena iz več medsebojno povezanih in z zakonom predpisanih sistemov nadzora nad posameznimi neželenimi učinki, ki se medsebojno dopolnjujejo in prekrivajo (6).

Pri uvajanju hemovigilance so največkrat uporabili t.im. "francoski model" . Najprej so sprejeli zakon, ki je predpisoval nadzor in prijavljanje neželenih učinkov transfuzije, potem pa so začeli izvajati hemovigilanco v praksi (2). SHOT (serious hazard of transfusion) program je oblika hemovigilance v Veliki Britaniji. Ustanovljen je bil s strani strokovnih medicinskih združenj. Njegovo izvajanje je prostovoljno na podlagi poklicne in strokovne zavezanosti medicinskega osebja. SHOT program so pozneje zdravstvene oblasti sprejele kot ustrezen način izvajanja hemovigilance in narekovale vsem bolnišnicam njegovo izvajanje. Značilnost SHOT programa je anonimnost prijavljanja neželenih učinkov. S tem so poskušali izključiti strah medicinskega osebja pred možnimi zakonskimi ali disciplinskimi sankcijami in tako zmanjšati njihov odpor ali nasprotovanje prijavljanju neželenih učinkov transfuzije, zlasti tistih, ki so posledica napake (4). Ker je sistem hemovigilance zahteven in obsežen, je bilo njegovo uvajanje v prakso večinoma postopno. Največkrat so najprej zasnovali mrežo hemovigilance, ki je delovala z manjšim obsegom, katerega so postopoma povečevali. Na Nizozemskem so hemovigilanco uvajali v treh fazah. V prvi so prijavljali in obravnavali le hude neželene učinke transfuzije (resna obolelost ali smrtni izid) v tretji fazi pa vse neželene učinke celotnega transfuzijskega postopka (5).

## Mreža hemovigilance

Mreža hemovigilance je praviloma centralizirana, piramidalne oblike in državnega pomena. Sestavljena je iz enega centralnega telesa na državni ravni (večinoma urad ali pravna oseba v sklopu ministrstva za zdravstvo) in mreže perifernih (lokalnih ter regionalnih) koordinatorjev (poročevalcev) zadolženih za hemovigilanco ter medicinskega osebja, ki je povezano z izvajanjem transfuzijske dejavnosti v bolnici in v transfuzijski ustanovi (slika 1). Od njihovega medsebojnega sodelovanja je odvisno učinkovito delovanje hemovigilance. Izbor ustrezne mreže hemovigilance je odvisen tudi od velikosti sistema transfuzijsko-bolnišnične oskrbe v državi.




Slika 1. Mreža hemovigilance (shematska slika)

## Glavne naloge

Medicinsko osebje, ki je povezano s transfuzijo krvi zaznava in prijavlja primere neželenih učikov transfuzije lokalnemu koordinatorju (poročevalcu) in lokalni transfuzijski ustanovi, ki je krvni pripravek zagotovila. Lokalni koordinator sam ali v sodelovanju s transfuziologom in bolnišničnim osebjem pripravi poročilo o neželenem učinku transfuzije ter ga posreduje regionalnemu koordinatorju ali neposredno v centralni urad, kjer se primer evidentira in vnese v podatkovno bazo. V transfuzijski ustanovi se ob prijavi opravi tudi sledenje komponente krvi, ki je bila povezana z neželenim učinkom transfuzije. Poročilo se lahko posreduje tudi lokalnim zdravstvenim oblastem, bolnišničnemu transfuzijskemu komiteju in oddelku, kjer se je dogodek zgodil. Ne glede na velikost sistema hemovigilance mora imeti posamezna institucija stalen dostop do svojih podatkov. Javljanje neželenih učinkov transfuzije je posebna odgovornost medicinskega osebja, ki je ločena od odgovornosti za medicinsko oskrbo bolnika.

V primerih neželenih učinkov transfuzije, ki lahko zajamejo več bolnikov ali krvodajalcev in so povezani s prenosom okužb, z uporabo vrečk, hranilnih in drugih raztopin ali z načinom predelave krvi in priprave krvnih pripravkov velja poseben način obveščanja in sporočanja. Najprej se obvesti transfuzijska ustanova, ki je izdala komponento krvi povezano z dogodkom. Tam se takoj opravi sledenje vpletene komponente krvi in se izločijo iz uporabe še preostali pripravki ali material, ki so lahko vzrok neželenega učinka. V primeru prenosa nalezljivih bolezni s pripravkom krvi ali ugotovitve pozitivnih izsledkov presejalnih testiranj na označevalce okužb, ki se prenašajo s krvjo pri krvodajalcih oziroma bolnikih je potrebno okužbe prijaviti ustanovi, ki ima nadzor nad nalezljivimi boleznimi. Zahteve po zaupnosti podatkov morajo biti v skladu z nacionalnimi predpisi.

Centralno zbiranje in analiza podatkov omogoča lažje in hitrejše tako odkrivanje in preprečevanje kot tudi raziskovanje neželenih učinkov transfuzije. Podatki se lahko uporabljajo na različnih ravneh: institucionalnih, regionalnih, nacionalnih in internacionalnih. Na podlagi analize shranjenih podatkov se oblikuje poročilo za določeno časovno obdobje (najpogosteje leto dni), ki odseva doseženo raven varnosti transfuzije v državi. Poročilo je osnova za določitev priporočil za preprečevanje nastanka nekaterih neželenih učinkov in nadaljnje delo v transfuzijski dejavnosti kot tudi politiko preskrbe s krvjo. Poročilo in priporočila se potem posredujejo vsem bolnišnicam in transfuzijskim ustanovam v sistemu hemovigilance.

Uspešno delovanje sistema hemovigilance je razvidno iz sledečega primera. Leta 1994 so v Angliji pri treh bolnikih s kronično mieloilčno levkemijo (KML), ki so bili zdravljeni s fludarabinom zabeležli nastanek bolezni presadka proti gostitelju po transfuziji pripravkov krvi. Po uvedbi SHOT programa so naslednjega leta prejeli še 3 poročila o enakih primerih. Zato so priporočali obvezno obsevanje krvnih pripravkov za transfuzijo bolnikom s KML, ki se zdravijo s fludarabinom. (7).

## Pogoji za učinkovito izvajanje hemovigilance

Dobro sodelovanje med transfuzijsko ustanovo in bolnišničnimi oddelki je pomembno, da se zagotovi popolna preiskava katerega koli neželenega učinka. Ob tem sodelujeta odgovorna zdravnika ali zdravnika zadolžen za hemovigilanco v transfuzijski ustanovi in bolnišničnem oddelku.

Porošilo o neželenih učinkih mora biti enotno v vseh pogojih in v vseh ustanovah, ki so povezane v sistem hemovigilance. Enotnost poročanja zajema poleg enotnega obrazca za poročanje tudi enotne definicije posameznih neželenih učinkov, enotno ukrepanje pri odkrivanju, potrjevanju in zdravljenju neželenih učinkov, kar lahko dosežemo le s skupnim izobraževalnim programom in politiko. Na ta način dosežemo enotno tolmačenje določenega dogodka.

Vodenja podatkov z računalniškim sistemom v klinični praksi in njihova povezava s računalniškimi sistemi v transfuzijskih ustanovah bo v veliki meri poenostavila in izboljšala zbiranje podatkov in poročanje o neželenih učinkih celotnega transfuzijskega procesa.

Izsledljivost krvodajalcev in bolnikov s sledenjem komponent krvi je zagotovljeno z možnostjo identifikacije bolnika, ki je prejel komponento krvi in obratno z možnostjo identifikacije vseh krvodajalcev, katerih kri je bila udeležena pri transfuzijskem dogodku. Potrebna je tudi aktivna povratna informacija o usodi vsake transfundirane komponente glede na prisotnost ali odsotnost neželenih učinkov transfuzije.

Sodelovanje in podpora države je pomembno za izdelavo legalnih osnov za dostop hemovigilance v bolnišnice, za zagotavljanje potrebnih materialnih sredstev in za aktivno sodelovanje v mreži hemovigilance na nacionalni ravni.

## Obseg in vrsta podatkov

Vzroki za nastanek neželenih učinkov lahko nastanejo na katerikoli stopnji celotnega postopka transfuzijske oskrbe. Zato zbiramo podatke o neželenih učinkih, ki se nanašajo tako na bolnika kot tudi na krvodajalca (tabela I).

Tabela 1. Vrsta neželenih učinkov transfuzije

| Pri prejemniku transfuzije |
|---|
| • Takojšnja reakcija med ali po transfuziji (hemoliza, vročinska reakcija, rdečica, urtikarija, alergija, anafilaktični šok, bakterijska okužba akutna okvara pljuč) |
| • Zapozneli neželeni učinki (hemoliza, bolezen presadka proti gostitelju po transfuziji, potransfuzijska purpura, zvečanje ALT, hemokromatoza) |
| • Prenos virusnih okužb |
| • Aloimunizacija na antigene eritrocitov, trombocitov in levkocitov |
| • Napačno transfundirana krvna komponenta |

| Pri krvodajalcu |
|---|
| • Neželeni učinki med dajanjem krvi |
| • Podatki vezani na izbor krvodajalcev (pogostost dajanja in vzroki odklona) |
| • Epidemiološki podatki o krvodajalcih s pozitivnimi izsledki presejalnih testov za določanje označevalcev okužb, ki se prenašajo s krvjo |

V hemovigilanci je potrebno, da zbrani podatki dajo čim bolj jasno in nedvoumno sliko o neželenem učinku transfuzije. Zelo obširni podatki lahko vzbujajo odpor za prijavljanje in poročanje o neželenih učinkih. Pomanjkljivi podatki pa onemogočajo ali omejujejo njihovo analizo in oceno ter primerjanje s podatki od drugod. Obseg in vrsta zbranih podatkov so delno določeni z zahtevo po enotnosti poročanja. Priporočilo Sveta Evrope določa najmanjši obseg poročila o neželenih učinkih, ki hkrati opredeljuje najmanjši obseg podatkov za zbiranje (3) (tabela 2).

**Tabela 2. Najmanjši obseg poročila**

| Inforamcije o prejemniku |
|---|
| Datum rojstva |
| Spol |
| Enotna številka |
| **Informacije o komponenti** |
| Enotna številka komponente |
| Vrsta komponente |
| Način priprave |
| Druge značilnosti (filtracija, obsevanje) |
| Pogoji in čas shranjevanja pred transfuzijo |
| **Informacije o stopnji neželenih učinkov** |
| (0) ni znakov |
| (1) takojšnje pojavljanje brez znakov življenjske ogroženosti in polne razvitosti |
| (2) takojšnje pojavljanje znakov z življenjsko ogroženostjo |
| (3) dolgotrajna obolelost |
| (4) smrt pacienta |
| **Informacije o povezanosti** |
| (0) ni povezave |
| (1) možna povezava |
| (2) verjetna povezava |
| (3) zanesljiva povezava |
| **Informacije o naravi dogodka** |
| Napaka v procesu |
| Nepričakovani medicinski učinek |
| Neželeni učinek brez napake |
| **Povzetek** |
| Opis dogodka in ukrepi |

V poročilu morajo biti podatki o prejemniku kot je datum njegovega rojstva, spol in identifikacijska številka bolnika in podatki o uporabljeni komponenti krvi, njena enotna številka, oznaka vrste krvne komponente, načina priprave, pogojev in časa hranjenja pred transfuzijo ter drugih značilnosti priprave. Sistem hemovigilance praviloma pokriva neželene učinke po transfuziji labilnih komponent krvi. Neželeni učinki zdravil iz krvi pa so nadzorovani s sistemom farmakovigilance. Jakost neželenih učinkov je razdeljena po stopnjah od 0-4. Odsotnost kliničnih znakov po transfuziji je označena s stopnjo 0. S stopnjo 1 je označen takojšnji pojav znakov brez življenjske ogroženosti in polne razvitosti. Takojšnji pojav znakov z življensko ogroženostjo pa je označen s stopnjo 2. Stopnja 3 predstavlja dolgotrajno obolelost in stopnja 4 pa smrt pacienta. Za oceno

vzročne povezanosti med neželenimi učinki in transfuzijo je predlagana gradacija od 0 – 3. Z oznako 0 – " ni povezave " - so označeni neželeni učinki povezani s transfuzijo vendar ni dokazov, da bi bila transfundirana komponenta vzrok njihovega nastanka. Če so učinki povezani s transfuzijo se lahko posledica transfuzije ali kakšnega drugega vzroka označijo z oznako 1 – " možna povezava ". Učinki, ki se pojavijo z zakasnitvijo in jih ne moremo razložiti z drugim vzrokom se označijo z oznako 2 – "verjetna povezava". Z oznako 3 – "zanesljiva povezava" se označijo učinki, ki so dokazano posledica transfuzije. Po vzroku nastanka so neželeni učinki razdeljeni na nepričakovane in tiste, ki so posledica napake v postopku transfuzije oziroma tiste, kjer napake ni bilo. Na koncu poročila je predviden tudi kratek povzetek, ki opisuje dogodek in potrebne ukrepe.

Ob načrtovanju hemovigilance je treba upoštevati predvideni najmanjši obseg poročila in specifične značilnosti sistema preskrbe s krvjo, bolnišničnega zdravljenja ter zakonodaje v posamezni državi.

## Omejitve hemovigilance

Raziskave so pokazale, da ostane določeno število neželenih učinkov transfuzije neprijavljeno (8). Vzrok temu je lahko napaka pri delu (namerno ali nenamerno neprijavljanje) ali pa so bili neželeni učinki brez kliničnih znakov (npr. transfuzija napačne vendar s prejemnikom skladne krvne komponente, imunizacija na antigene krvnih celic). Pogosto so pomanjkljivi tudi podatki o porabi krvnih pripravkov in o številu prejemnikov transfuzije, ki so potreben imenovalec pri izračunu pogostnosti neželenih učinkov.

## Stanje pri nas

Že leta 1968 smo v Sloveniji imeli Strokovno navodilo o ravnanju s krvjo na bolnišničnih oddelkih in o pripravi na transfuzijo, ki je določalo postopke ob neželenih učinkih transfuzije pa tudi način njihovega prijavljanja in poročanja v transfuzijsko ustanovo, ki je krvni pripravek izdala (9). Obstajal je tudi poseben obrazec za poročanje o izidu transfuzijskega zdravljenja, ki je zajemal tudi neželene učinke. Navodila za delo v transfuzijski dejavnosti iz leta 1992 tudi obravnavajo prijavljanje in poročanje o neželenih učinkih transfuzije (10). Kljub temu sistem poročanja o neželenih učinkih transfuzije ni zaživel v praksi najverjetneje zato, ker ni bil zasnovan kot enoten sistem na državni ravni in ni bil zakonsko obvezen. V praksi smo zasledili le posamezene sporadične primere poročanja o hudih neželenih učinkih in nekatere retrospektivne raziskave ali poročila. Tako so med letom 1989 in 1992 v eni bolnišnici ugotovili 4 primere neskladne transfuzije, ki so se končali brez smrtnega izida, po transfuziji 12.394 enot pripravkov eritrocitov 3846 bolnikom (11).

Uvajanje hemovigilance v transfuzijsko dejavnost se je začelo šele leta 1997 s Projektom reorganizacije transfuzijske službe v Sloveniji. V njem je bilo načrtovano uvajanje hemovigilance v sklopu sistema zagotavljanja kakovosti (12). Po vzoru na Francijo in na podlagi lastnih izkušenj smo hemovigilanco uredili z Zakonom o preskrbi s krvjo (2). Naslednji korak je izbor najustreznejše organizacijske mreže, načina prijavljanja in poročanja kot tudi določitev dinamike uvajanja glede na obseg podatkov, ki jih bomo zbirali. Hkrati pa je potrebno zagotoviti v sklopu Ministrstva za zdravstvo centralno vodenje, hranjenje podatkov in poročanje o neželenih učinkih transfuzije. Določiti je treba tudi katero strokovno telo bo analiziralo poročila in pripravilo ustrezne ukrepe in priporočila za nadaljnje delo. Izvajanje hemovigilance bomo tudi uredili s pravilnikom, ki bo določal tudi enoten obrazec za poročanje o neželenem učinku transfuzije.

## Zaključki

Sistem hemovigilance se je v praksi uveljavil kot sestavni del sistematičnih ukrepov zagotavljanja kakovosti, ki imajo za cilj povečanje varnosti transfuzije pripravkov krvi.

Tudi pri nas smo na podlagi izkušenj drugih držav z zakonom določili oblikovanje enotnega, centraliziranega sistema hemovigilance.

V nadaljevanju je treba izbrati najustreznejši način poročanja in organizacije hemovigilance, ustanoviti njeno mrežo in zagotoviti centralno vodenje ter določiti načine in organe za strokovno ukrepanje.

Ob načrtovanju hemovigilance je treba upoštevati strokovna priporočila in specifične značilnosti sistema preskrbe s krvjo, bolnišničnega zdravljenja ter zakonodaje v državi. Posebej je treba proučiti možnosti uporabe računalniškega sistema za njeno izvajanje.

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# Vloga zdravnika pri postopkih transfuzije krvi

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*Pisno spremljanje uporabe krvi in krvnih pripravkov (33. člen) ter tudi biotehnoloških nadomestkov za kri obsega od:*

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## Uvod

Novi Zakon o preskrbi s krvjo, ki velja od julija letos določa načine zbiranja človeške krvi in njenih pripravkov, preskrbo prebivalstva z njimi ter uporabo krvi in pripravkov krvnih celic ter pripravkov plazme. V zakonu je opredeljena neposredna in posredna vloga zdravnika specialista transfuzijske medicine v Zavodu Republike Slovenije za transfuzijsko medicino in oddelku za transfuzijsko medicino v bolnišnicah, na novo pa neposredna vloga zdravnika, ki uporablja kri in pripravke krvi za zdravljenje, kar bom obravnaval v sestavku.

## Novosti Zakona o preskrbi s krvjo

Sprejem Zakon o preskrbi s krvjo je določil predvsem tri novosti zdravnikom uporabnikom krvi in krvnih pripravkov, ki smo jih morali takoj začeti izvajati:

1. pred operativnim posegom, pri katerem se predvideva večja izguba krvi, je zdravnik dolžan bolniku ponuditi možnost avtologne transfuzije krvi (15. člen).
2. pred prejetjem transfuzije krvi in krvnih pripravkov mora bolnik pisno potrditi, da je bil obveščen o transfuziji in njenih posledicah in da je vanjo privolil (32. člen).
3. Kakovost pri uporabi krvi in krvnih pripravkov predpisuje 30. člen, ki določa da mora zdravnik zagotoviti smotrno in kakovostno rabo krvi in krvnih pripravkov po sodobnih načelih transfuzijske medicine, ter pisno voditi postopek transfuzije krvi in krvnih pripravkov z vrednotenjem želenih in neželenih učinkov oziroma zapletov.

Pri smotrni in kakovostni rabi krvi mora zdravnik oceniti stopnjo nujnosti, vrsto in količino naročene krvi in krvnih pripravkov, ter pridobiti podatke o morebitnih predhodnih transfuzijskih reakcijah.

Za nadzor izvajanja celovite kakovosti pri uporabi krvi in krvnih pripravkov se ustanove v vseh bolnišnicah, ki uporabljajo kri in krvne pripravke Bolnišnični transfuzijski odbori, do sedaj Delovne skupine za kakovostno rabo krvi in krvnih pripravkov.

- pisne potrditve oziroma privolitve bolnika za transfuzijo krvi,
- izsledek krvne skupine,
- izsledke laboratorijskih preiskav pred in po zdravljenju s krvjo in krvnimi pripravki, ki zagotavljajo oceno želenih in morebitnih neželenih učinkov zdravljenja.

Pisna dokumentacija mora omogočiti izsleditev vsakega darovalca krvi oziroma krvnega pripravka in prejemnika.

Kazalce spremljanja uporabe krvi in krvnih pripravkov določa 34. člen. Zdravnik mora ob vsaki uporabi krvi in krvnih pripravkov zabeležiti naslednje podatke:

- identifikacijsko številko bolnika ali priimek in ime, datum rojstva in naslov,
- številko izsledka krvne skupine bolnika,
- enotno številko pripravka in njegovo oznako, proizvajalca, količino in vsebnost
- datum in uro uporabe in
- druge predpisane podatke.

Neželene učinke uporabe krvi in krvnih pripravkov določa 36.

Zdravnik mora pri pojavu neželenih učinkov takoj obvestiti odgovorno osebo Bolnišničnega transfuzijskega odbora, ta pa odgovorno osebo oddelka za transfuzijsko medicino v bolnišnici.

Prav tako obvestimo osebo za spremljanje neželenih učinkov zdravil Urada R Slovenije za zdravila.

Obvestilo mora vsebovati oznako pripravka, ime proizvajalca, podatke osebe, pri kateri se je neželeni učinek pojavil ter skrbno opisani neženi učinek.

## Odgovornosti zdravnika pred in med transfuzijo krvi

Ukrepi pred transfuzijo krvi

1. Pridobitev soglasja bolnika za načrtovano transfuzijo krvi in krvnih pripravkov.
2. Pridobitev podatkov o morebitnih predhodnih transfuzijskih reakcijah.
3. Bolniku ponuditi možnost avtologne transfuzije krvi.
4. Smotrno naročati kri in krvne pripravke, tako glede na nujnost uporabe, kot vrsto in količino pripravkov.
5. Zagotovitev nadzora nad odvzemom krvi za določitev krvne skupine.
6. Identifikacija bolnika pri jemanju vzorcev krvi

   Preveriti mora podatke o bolniku na način, da ga vpraša (ime, priimek, datum rojstva in enotna nova medicinska oznaka, pri novorojencih pa še spol in identifikacijska številka iz zapestnega traku) in na etiketi epruvete ter na transfuzijski naročilnici, ki jo mora izpolniti in podpisati za potrditev identitete bolnika. Pri bolnikih neznane identitete uporabimo za prepoznavo enotno identifikacijsko številko iz zapestnega traku. Vzorce krvi za določitev krvne skupine ali navzkrižnega preskusa, moramo vedno zavrniti, če nimajo ustrezne oznake za prepoznavo.
7. Serološke preiskave krvnih skupin

   Napotiti mora kri v laboratorij transfuzijske medicine za določitev krvne skupine, presejalnih preskusov za protitelesa in preskusov skladnosti pred transfuzijo eritrocitnih pripravkov.

Če je bolnikovo življenje ogroženo izjemoma izvajamo preiskave vzporedno s transfuzijo krvnih pripravkov, običajno pa vedno pred transfuzijo.

## Določitev krvne skupine

Določitev krvne skupine ABO in Rh(D) in po potrebi tudi drugih krvnih skupin napravimo praviloma vedno pred transfuzijo. Nadalje se priporoča , da opravimo presejalni preskus na protitelesa, za odkrivanje nepričakovanih eritrocitnih protiteles, skupaj z določitvijo krvne skupine.

Običajno se preiskave opravijo pravočasno pred pričakovano transfuzijo krvnih pripravkov oziroma pred načrtovanim kirurškim posegom.

Laboratorij mora določati krvne skupine na zanesljiv in standardizirani način, ki obsega dvojno preverjanje podatkov ob izdaji izsledkov preiskav krvne skupine in drugih seroloških preiskav, ki se priložijo v bolnikovo medicinsko dokumentacijo.

## Preskusi skladnosti krvi

Zagotoviti mora preskuse skladnosti. Pri transfuziji eritrocitnih pripravkov mora biti zagotovljena skladnost med darovalcem in prejemnikom. Preskus skladnosti ni priporočljivo izvajati iz vzorca krvi, ki je bil prvotno uporabljen za določitev krvne skupine, temveč z novim vzorcem, ki je bil odvzet največ 4 dni pred predlagano transfuzijo.

Osnova za skladnost je pravilno določena krvna skupina ABO in Rh(D) pri darovalcu in prejemniku transfuzije. Kadar so v bolnikovem krvnem obtoku prisotna nepričakovana eritrocitna protitelesa, moramo za transfuzijo izbrati takšne eritrocite, ki nimajo odgovarjajočih antigenov. Preskus skladnosti med darovalčevimi eritrociti in prejemnikovim serumom moramo opraviti vedno, ko so prisotna nepričakovana eritrocitna protitelesa. Priporoča se kot rutinski postopek tudi v primerih, ko protiteles niso zaznali. Preskušanje pa lahko opustimo, če obstajajo drugi načini, kot tipiziranje ali presejalno preskušanje, ki zagotavljajo varnost.

## Ukrepi med transfuzijo krvi

1. Varnostni ukrepi

Z dravstveni delavec, ki daje transfuzijo krvnih pripravkov je odgovoren za kontrolo identitete in za druge varnostne ukrepe.

Pred transfuzijo krvi preverimo identiteto prejemnika, vprašamo ga po imenu, priimku, datumu rojstva in identifikacijski številki iz zapestnega traku. Pred transfuzijo mora zdravstveni delavec preveriti, da je pripravljen ustrezen transfuzijski set vskladu s priporočili proizvajalca. Priporoča se, da posameznega transfuzijskega seta ne uporabljamo več kot 6 ur. Pred transfuzijo skrbno preverimo izgled krvnih pripravkov.

Preverimo skladnost med prejemnikom in enoto krvnega pripravka na način da:

- primerjamo podatke o identiteti prejemnika s podatki laboratorijskega preskusa skladnosti,
- primerjamo krvno skupino prejemnika na izvidu in krvno skupino označeno na etiketi enote krvnega pripravka,
- preverimo rok uporabe enote krvnega pripravka,
- zabeležimo identiteto bolnika.

Identifikacijska številka in vrsta krvnega pripravka morata biti vpisani v bolnikovi klinični dokumentaciji tako, da lahko po potrebi izsledimo darovalca krvnega pripravka.

Pred transfuzijo določimo ob bolniku krvno skupino na ploščici.

2. Klinični nadzor

Vsaj prvih 15 minut transfuzije krvnega pripravka moramo bolnika skrbno spremljati. Zagotoviti moramo priporočeno hitrost dajanja transfuzije.

3. Segrevanje krvi

Pred transfuzijo krvnega pripravka moramo zagotoviti ustrezno temperaturo krvi. Hitra transfuzija hladne krvi je lahko nevarna. Uporabljeni grelec moramo skrbno nadzorovati, da se zagotovi ustrezna temperatura krvi.

4. Dodajanje zdravil in infuzijskih raztopin pripravkom krvi

Transfuziji krvnega pripravka ne smemo dodati zdravilo ali drugo infuzijsko raztopino. še posebej ne smemo dodajati raztopine, ki vsebuje kalcij ali koncentrirano glukozo.

5. Ravnanje z zmrznjenimi krvnimi pripravki

   Z zmrznjenimi pripravki plazme moramo ravnati previdno, ker je embalaža lomljiva in lahko pri nizkih temperatutah poči. Pred uporabo jih odtajamo, pregledamo da je vsebina raztopljena in da vrečka ni poškodovana. Vrečke, ki puščajo, moramo zavreči. Odmrznjeni pripravek transfundiramo v najkrajšem času.

6. Nevarnost zračne embolije

   Preprečiti moramo vstop zraka v transfuzijski sistem zaradi nevarnosti zračne embolije.

7. Učinkovitost transfuzije krvnih pripravkov

   Ocenimo iz izsledkov preiskav krvi, ki jih opravimo pred in po transfuziji.

8. Neželeni pojavi transfuzije krvi

   Zdravnik mora pri pojavu neželenih učinkov transfuzije krvnih pripravkov, le te skrbno zapisati in takoj obvestiti odgovorno osebo.

Neželeni pojavi se lahko pojavijo takoj med transfuzijo krvnega pripravka ali neposredno po njej ali šele po nekaj urah ali dneh. Hude neželene pojave moramo raziskati, blažje pa le po presoji odgovorneg zdravnika.

Kadar se pojavijo med in po transfuziji krvnih pripravkov klinično pomembni neželeni pojavi, kot mrzlica, vročina, težave pri dihanju, šok, hipotenzija ali bolečina v ledvenem predelu moramo:

- preveriti krvne skupine ABO in Rh na etiketi enote krvi in na izvidu krvne skupine. Če so prisotna nepričakovana protitelesa zunaj sistema ABO in Rh, moramo preveriti, če je bila uporabljena skladna kri.
- vzorec krvi odvzet po transfuziji, enoto krvi s sistemom za transfuzijo in spremljajoče epruvete pošljemo v preiskavo.

Pri ponavljajočih febrilnih nehemolitičnih reakcijah po transfuziji krvi nadaljujemo s pripravki eritrocitov z odstranjenimi levkociti, po možnostipo tem ko se preveri prisotnost protiteles proti levkocitnim antigenom. Pri transfuzijskih reakcijah po koncentriranih trombocitih uporabljamo nesteroidna protivnetna zdravila. Pri odloženih neželenih pojavih preverimo vzroke, kot aloimunizacija in prenos bolezni.

Med zdravnikom in ustanovami za transfuzijsko medicino mora obstojati sodelovanje, da se olajša raziskovanje možnih prenešenih okužb prejemnika s transfuzijo, ko se ugotovi serokonverzija pri darovalcu krvi.

Skrben nadzor in svetovanje sta potrebna tudi, če je prišlo do aloimunizacije proti transfundiranim celicam.

## Bolnišnični odbor za transfuzijsko medicino

Bolnišnične odbore za transfuzijsko medicino je potrebno ustanoviti v bolnišnicah, kjer pri zdravljenju uporabljajo kri in krvne pripravke.

Sestavljajo jih zdravniki specialisti transfuzijske medicine in drugi zdravniki specialisti ter medicinsko in administrativno osebje, ki pri zdravljenju uporabljajo kri in krvne pripravke.

Naloge Bolnišničnega odbora za transfuzijsko medicino so:

- določi in nato nadzira smotrno rabo krvi in krvnih pripravkov v bolnišnici,
- vzpodbuja transfuzijo le tiste sestavine krvi, ki manjka,
- vrednoti želene in neželene učinke oziroma zaplete in
- po potrebi sprejemajo ukrepe za izboljšanje stanja.

## Zaključki

Kljub temu, da nam je hiter razvoj transfuzijske medicine omogočil zagotoviti zadostno količino krvi, pripravkov krvnih celic in plazme, pa so še vedno potrebna neprestana intenzivna prizadevanja za varno transfuzijo krvi, ki je danes glavna naloga transfuzijske medicine.

Kljub vsem zagotovilom o varnosti transfuzije krvi, pa priporočamo uporabiti kri, pripravke krvnih celic in plazme le takrat, ko nimamo na voljo drugih načinov zdravljenja.

Osnovno načelo transfuzije je, da nadomeščamo le tisto sestavino krvi, ki manjka. Druge sestavine krvi so lahko ne le odveč, temveč celo škodljive. Ker imajo krvne celice omejeno življensko dobo v krvnem obtoku je običajno učinek transfuzije le začasen.

S transfuzijo krvi pa so lahko povezani zgodnji in pozni zapleti, ki se lahko končajo celo z bolnikovo smrtjo.

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# "Vloga medicinske sestre pri postopkih transfuzije krvi"

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## Vloga medicinske sestre v zdravstvenem sistemu

Vloga medicinske sestre je v zadnjem stoletju doživljala številne spremembe, ki so temeljile na razvoju celotnega sistema zdravstvenega varstva ljudi. Pristojnosti nosilk poklica so se širile z dvigovanjem strokovne izobrazbe, ki je sledilo hitremu razvoju znanosti na zdravstvenem področju.

V sedanjem zdravstvenem sistemu ima dejavnost zdravstvene nege pomembno vlogo. Medicinske sestre in zdravstveni tehniki, kot največja skupina zdravstvenih delavcev, predstavljajo velik človeški in intelektualni potencial. S svojim strokovnim delom pospešujejo in dvigujejo kakovost in večjo učinkovitost zdravstvene obravnave bolnikov. Samostojno ugotavljajo potrebe, načrtujejo, organizirajo, izvajajo in ocenjujejo uspešnost izvajanja zdravstvene nege bolnika s ciljem, da v najkrajšem možnem času dosežejo njegovo neodvisnost. Tesno sodelujejo z zdravnikom in ostalimi zdravstvenimi delavci in sodelavci v zdravstvenem timu pri izvajanju programa diagnostike, zdravljenja in rehabilitacije bolnikov, pri izobraževalnem, razvojno raziskovalnem procesu ter vodenju organizacijskih enot in zavodov.

Z dodatnim izobraževanjem na lastnem strokovnem področju in na področju sociološkiih, filozofskih, organizacijskih, pedagoških in ekonomskih znanosti in v zadnjem času tudi pravnih znanosti, so medicinske sestre izoblikovale spremenjeno filozofijo svojega delovanja. Ta temelji na vrednotah zdravstvene nege in etičnih načelih s povdarkom na celoviti, humani obravnavi bolnika in njegovih potreb, z upoštevanjem njegovih človečanskih in bolnikovih pravic. Povdarek je na preprečevanju dejavnikov tveganja in zagotavljanju varne in učinkovite zdravstvene nege.

Mednarodno poklicno združenje in nacionalno združenje medicinskih sester in zdravstvenih tehnikov Slovenije sta oblikovala poklicni kodeks, katerega načela zavezujejo izvajalce pri njihovem delu. Vloga in pristojnosti medicinskih sester so jasno opredeljene, za naloge prevzemajo medicinske sestre polno odgovornost. Pri delu jih zavezujejo pravila o dolžnostih in odgovornostih kot moralne norme, poklicno deontološke norme in pravne norme.

Medicinske sestre in zdravstveni tehniki so za izvajanje zdravstvene nege bolnikov pristojni, ker so zato strokovno izobraženi in ustrezno usposobljeni. Za izvajanje zdravstvene nege bolnikov prevzemajo :

- **osebno moralno odgovornost** za svoje ravnanje,
- **strokovno poklicno deontoloko odgovornost** za izvajanje dejavnosti po veljavnem poklicnem kodeksu , smernicah in strokovnih standardih Razširjenega strokovnega kolegija zdravstvene nege pri Ministrstvu za zdravstvoin Nacionalnega poklicnega združenja,
- **pravno odgovornost** kot:
- disciplinsko odgovornost, ki je določena z disciplinskim pravilnikom,
- odškodninsko odgovornost za povzročeno škodo,
- kazensko materialno odgovornost.

**Področje odgovornosti opredeljuje tudi 55. člen Zakona o zdravstveni dejavnosti RS** s temelji za odgovornost zdravstvenega delavca s pogoji:

- vsak zdravstveni delavec lahko samostojno opravlja delo, za katero ima ustrezno izobrazbo, je zanj usposobljen ter ima na razpolago ustrezno opremo.

Strokovni regulativi in smernice razvoja zdravstvene nege, ki opredeljujejo vlogo zdravstvene nege v zdravstvenem sistemu, na nacionalni ravni so:

- Kodeks medicinskih sester in zdravstvenih tehnikov Slovenijev iz leta 1994 ,
- Deklaracija o bolnikovih pravicah, ki jo je izdala Svetovna zdravstvena organizacije za Evropo,
- Dolgoročni program splošnega razvoja zdravstvene nege iz leta 1993,
- Usmeritve razvoja zdravstvene nege v luèi zdravstvenih reform v RS 1996
- Strokovni standard "Razmejitev zdravstvene nege", ki govori o temeljnih določilih, pristojnostih, nalogah, načinu in delitvi dela v zdravstveni negi, ki je bil potrjen in sprejet na 63. seji Zdravstvenega sveta Ministrstva za zdravstvo, 14.3. 1996.

Izpostavlja delitev dela v negovalnem timu, odgovornost in strokovnost medicinske sestre in zdravstvenega tehnika, dela in naloge in klasifikacijo intervencij v zdravstveni negi. V skupino intervencij v zvezi z dajanjem zdravil sodi tudi zdravljenje s krvjo in krvnimi pripravki, ki pa ni eksplicitno navedeno, ker sodi v delokrog zdravnika.

- Nacionalne smernice za kakovost v zdravstveni negi
- Strokovni standardi in pravilniki za izvajanje procesa zdravstvene nege

Medicinske sestre in zdravstveni tehniki sodelujejo z zdravnikom v zdravstvenem timu v procesu diagnostike zdravljenja in rehabilitacije. Če medicinska sestra prevzame po naročilu zdravnika izvajanje medicinsko tehničnih posegov, za katere je pristojen in končno odgovoren zdravnik, ima medicinska sestra na temelju prenešenih pooblastil nanjo, podrejeno samostojnost. To pomeni , da nosi odgovornost za pravilno izvedbo zdravnik, pa čeprav postopka ni sam opravil. Zato je v zdravstvu pomembno spoštovanje temeljnega načela pri delitvi dela vsak zdravstveni delavec sme opravljati samo tisto delo, ki ga je zmožen obvladati po svoji izobrazbi in ga zares obvlada po svoji izkušenosti. Čista delitev dela z vso odgovornostjo pomeni največjo stopnjo varnosti za bolnika in za zdravstvenega delavca.

## Zagotavljanje pogojev za kakovostno zdravljenje s krvjo in krvnimi pripravki v zdravstvenih zavodih

Zdravstvene ustanove, ki izvajajo zdravljenje bolnikov s krvjo so dolžne zagotavljati pogoje za varno in kakovostno izvajanje zdravljenja na osnovi sprejetih zakonski aktov in regulativov. Opredeliti morajo odgovornost za kakovost na vseh ravneh vodenja, zagotoviti delitev dela med zdravstvenimi delavci z opisi delokrogov, zagotoviti zadostno število zaposlenih z zahtevano izobrazbeno strukturo in usposobljenostjo, učinkovito organizacijo dela, sredstva za neprekinjeno strokovno izobraževanje in usposabljanje ter ustrezen informacijski sistem za stalno zbiranje podatkov s programsko opremo, za potrebe primerjanja in ugotavljanja uspešnosti izidov zdravljenja. Ne nazadnje je za dobro delo potrebna tudi standarizirana delovna oprema, ki sledi razvoju in potrebam stroke.

V Sloveniji so bili v letu 2000 na osnovi priporočila SVETA EVROPE Odbora Ministrov, katerega cilj je doseči večjo enotnost med državami članicami, sprejeti skupni ukrepi na področju preskrbe s krvjo:

**Zakon o preskrbi s krvjo**, ki po poglavjih opredeljuje:

- namen zakona, preskrbo s krvjo in opredelitev pojmov,
- krvodajalstvo, zbiranje krvi in odvzem krvi,
- uporabo in ravnanje s krvjo,
- delovanje Strokovnega sveta za preskrbo s krvjo in vrste nadzora pri Ministrstrvu za zdravstvo,
- kazenske določbe in končne določbe.

**Priporočilo o pripravi, uporabi in zagotavljanju kakovosti komponent krvi**, ki ga je izdal Zavod RS za transfuzijo krvi, v sodelovanju z Informacijsko Dokumentacijskim Centrom Sveta Evrope, na osnovi priporočila Odbora Ministrov št. R ( 95 ) 15. Določa dobro proizvodno prakso in pripravo komponent krvi, vrste komponent krvi, laboratorijske postopke in transfuzijsko prakso .

## Oprema in pripomočki za shranjevanje, prenos, dajanje krvi in krvnih pripravkov

Zdravstveni zavodi, ki izvajajo zdravljenje bolnikov s krvjo in krvnimi pripravki so dolžni opremiti prostore za začasno shranjevanje krvi in krvnih pripravkov z ustreznimi hladilniki za začasno shranjevanje krvi. Ti omogočajo stalno kontrolo temperature z grafičnim zapisom, imajo notranji termometer in termostat, zvočno in vidno signalno napravo za visoke in nizke temperature od $+2^0$C do $+6^0$C.

Za uporabo sveže plazme so primerni zamrzovalniki za shranjevanje pod – $30^0$C in se uporabljajole za zamrzovanje krvnih pripravkov po navodilih.

Ne smejo se uporabljati za potrebe gospodinjstva.

Za gretje krvi in krvnih pripravkov se uporabljajo suhi grelci, za toplenje zamrznjene plazme pa sodobni vodni grelci. Vodne kopeli starejše vrste, ki so še v uporabi za gretje krvnih pripravkov, so ob slabem vzdrževanju higiensko oporečni in vir okužb. Oprema za gretje se uporablja po navodilu ZTK.

Za prenos krvi in krvnih pripravkov se uporabljajo hladilne torbe iz trde plastike s stojali za zaščito krvnih vzorcev in vrečk.

Za transfuzijo krvi se uporabljajo primerne i.v. kanile in sterilni transfuzijski sistemi s filtrom od 170 do 200 mikrometrov. Po potrebi se za pospešeno dajanje transfuzije uporabljajo sistemi za hitro transfuzijo z balonom in manšete za pospeševanje transfuzije po navodilih.

## Izobraževanje zaposlenih medicinskih sester za spremljanje sodobnih strokovnih smernic.

Vodstva zavodov in strokovno organizacijskih enot v zdravstvenem zavodu so odgovorna za zagotavljanje rednega funkcionalnega izobraževanja zaposlenih, preverjanja teoretičnega znanja s preizkusom znanja in usposobljenosti za delo najmanj na tri leta.

Medicinske sestre, ki izvajajo postopke s krvjo in sodelujejo z zdravnikom pri zdravljenju s krvjo in krvnimi pripravki, morajo imeti višjo oz. visoko strokovno izobrazbo, večletne izkušnje pri delu z bolniki, kjer poteka zdravljenje s krvjo in dodatna znanja iz področja transfuzijske medicine.

Za spremljanje sodobnih strokovnih smernic in novih spoznanj se izvajalci zdravstvene nege udeležujejo strokovnega usposabljanja in izobraževanja, ki ga izvaja Zavod za transfuzijo krvi v Ljubljani.

Dodatna znanja, ki jih morajo pridobiti medicinske sestre za višjo strokovno usposobljenost in prevzemanje odgovornosti za izvajanje nalog v zvezi z zdravljenjem s krvjo in krvnimi pripravki so:

- sestava in značilnosti krvi, krvne skupine in podskupine,
- zbiranje krvi in dobra proizvodna praksa,
- obvezna testiranja krvi na prisotnost povzročiteljev bolezni, skladnost ABO in RhD sistema,
- napake, ki jih lahko povzročijo ABO neskladne transfuzije krvi,
- nevarnosti transfuzije in prepoznavanje neželenih reakcij na transfuzijo,
- izvajanje standariziranih postopkov zdravstvene nege v zvezi s transfuzijo,
- sodelovanje medicinske sestre in zdravnika pri izvajanju transfuzije krvi,
- nadzorovanje in opazovanje bolnika ter poročanje o spremembah zdravstvenega stanja bolnika, izpolnjevanje negovalne dokumentacije in ravnanje z predpisano dokumentacijo,
- ukrepanje ob pojavu znakov transfuzijske reakcije,
- previdnostni ukrepi pri transfuziji krvi in krvnih pripravkov in posebne zahteve pri pripravi pripravkov in pripomočkov,
- pravilno ravnanje z različnimi krvnimi pripravki – naročanje, prenos, začasno hranjenje na bolniškem oddelku ali posebni Enoti za hranjenje krvi in krvnih pripravkov, priprava pred aplikacijo, vračanje v depo ali na ZTM,
- ravnanje z odpadki.

## Posebnosti pri transfuziji krvi in rokovanju s krvnimi pripravki

V skladu z navodili, ki so opisani v "Priporočilih o pripravi, uporabi in zagotavljanju kakovosti komponent krvi" mora medicinska sestra v praksi posebej skrbno ravnati s krvjo in krvnimi pripravki , ki se naročajo na ZTK, zagotavljati ustrezen transport krvnih pripravkov iz transfuzijske enote, pripravo krvnih komponent za uporabo in preverjanje izgleda krvnega pripravka, ev. poškodbe vrečk ipd. Zdravnik in medicinska sestra , ki sodelujeta pri postopkih s krvjo morata upoštevati navodila za uporabo za:

- polno kri in koncentrirane eritrocite,
- koncentrirane trombocite,
- svežo zmrznjeno plazmo,
- oprane eritrocite, eritrocite z odstranjenimi levkociti, granulocite,
- drugo

## Napake, ki zmanjšujejo uspešnost zdravljenja s krvjo

Posebno pozornost mora biti namenjena preprečevanju napak v praksi in dejavnikov tveganja.

Če pride do zamenjave krvi, ko prejemnik dobi kri neskladne skupine ali ko RhD negativni prejemnik dobi RhD pozitivno kri, se pojavi transfuzijska reakcija, ki je posledica vezave protiteles na antigene. Posledica je hemoliza razpad eritrocitov. Taka reakcija je življenjsko nevarna, zato je pred transfuzijo krvi potrebno zadovoljiti vsem previdnostnim ukrepom, da do zamenjave krvi ali vzorca ne pride.

Najpogostejše napake pri postopkih s krvjo so:

- pri prepoznavanju bolnika - napačni osebni podatki (ne preverjamo bolnikovih podatkov in osebnega dokumenta, obstoja možnost izposoje, bolnik ni pravi! bolnik je neoznačen in nima podatkov, brez zapestnice - štev. primera hospitalizacije)
- pri postopkih odvzema vzorca bolnikove krvi za določitev krvne skupine in RhD faktorja oz. pri idenfikaciji bolnika (napačen bolnik ob odvzemu ali prejemu krvi), (napačno označen vzorec bolnikove krvi- nalepka), (zamenjane epruvete s krvjo pri odvzemu krvnih vzorcev večim bolnikom hkrati)
- pri naročanju krvi (niso označene posebne zahteve),
- pri preverjanju podatkov o skladnosti bolnikove krvne skupine ali prisotnosti protiteles, skladnosti naročila z vrsto krvnega pripravka v vrečki pri dvigu iz Enote za hranjenje krvi in krvnih pripravkov,
- zaradi nepopolnih podatkov o bolniku , potrebni količini in vrsti krvnih pripravkov pri naročanju po telefonu.

## Nadzorovanje bolnika med transfuzijo in prepoznavanje neželenih reakcij

Pri zdravljenju bolnika s krvjo in krvnimi pripravki sodelujeta zdravnik in medicinska sestra v skladu s pristojnostmi ter sprejetimi strokovnimi standardi, ki sledijo najsodobnejšim znanstvenim spoznanjem. Ob upoštevanju vseh varnostnih zahtev se pri transfuziji krvi lahko pojavijo neželene reakcije, ki so za bolnika nenevarne in brez posledic, in nevarne, ki lahko povzročijo poslabšanje zdravstvenega stanja ali celo ogrozijo bolnikovo življenje. Kljub naglemu razvoju transfuzijske medicine še vedno obstoja verjetnost za prenos bolezni preko transfuzije krvi.

Življensko nevarne reakcije se zaradi neskladnosti krvi se največkrat pojavijo v prvih 15 minutah transfuzije. Zato morata biti zaradi nadzora in nujnega ukrepanja prvih 15 minut dajanja transfuzije pri bolniku obvezno prisotna zdravnik in medicinska sestra. Če po preteku 15 minut zdravnik ne opazi neželenih reakcij z nadzorom transfuzije in opazovanjem bolnika nadaljuje medicinska sestra. Ob prvem pojavu znakov reakcije na transfuzijo je dolžna o tem obvestiti zdravnika in znake reakcije vpisati v negovalno dokumentacijo. Glede na vrsto reakcije ukrepa po navodilih, ki so sprejeta na strokovnih organih in v soglasju z transfuzijskim odborom zavoda.

Medicinska sestra je sposobna prepoznati naslednje reakcije, ki se pojavljajo med dajanje transfuzije in krvnih pripravkov:

- akutna in pozna hemolitična reakcija zaradi neskladnosti v krvni skupini ABO in RhD,
- alergična reakcija, ki nastane zaradi prisotnosti protiteles proti plazemskim beljakovinam,
- reakcijo s povišanjem telesne temperature, ki nastane kot reakcija antigena na protitelo zaradi protiteles proti levkocitom ali trombocitom,
- reakcije na prenešeno okužbo pri nepravilnem rokovanju s krvnim pripravkom,
- preobremenitev krvnega obtoka,

## Pristojnost medicinske sestre, zdravstvenega tehnika, kurirja pri postopkih transfuzije krvi in krvnih pripravkov

V 55. členu Zakona o zdravstveni dejavnosti je podana temeljna zahteva po jasni delitvi dela v zdravstvenem timu, glede na različno stopnjo strokovne usposobljenosti in izkušenosti in vsebino nalog. Vnaprej določene naloge, ki jih opredeljuje strokovni standard opredeljujejo tudi dolžnosti in obveznosti za katere člani tima prevzemajo odgovornost. Strokovni standard zmanjšuje stopnjo tveganja in zagotavlja večjo varnost za bolnika in za izvajalca. Velja načelo, da nihče ne more prenesti na drugega svojih lastnih dolžnosti niti odgovornosti.

Pristojnosti – odgovornosti medicinske sestre pri naročanju krvi so:

- informiranje bolnika o načrtovanih postopkih zdravstvene nege,
- pravilna prepoznava bolnika pred odvzemom krvi,
- pravilen odvzem krvi za transfuzijske preiskave,
- pravilna označitev epruvete z bolnikovo krvjo z nalepko tik po odvzemu krvi,
- pravilna označitev z nalepkami in izpolnitev vseh predpisanih dokumentov, datum, žig, čitljiv podpis v skladu s pristojnostjo (podatki o bolniku) na transfuzijsko naročilnico, transfuzijski karton, spremni dokumenti za prenos krvnih vzorcev na ZTM,
- beleženje postopka v negovalno dokumentacijo,
- obveščanje ZTM o prihodu bolnika za odvzem krvi za avtologno transfuzijo, posredovanje informacij bolniku in svetovanje v zvezi z avtologno transfuzijo,
- zdravstveno vzgojno delo z bolnikom in svojci

Pristojnosti – odgovornosti medicinske sestre pri dajanju krvi in nadzoru krvi ob upoštevanju "petih pravil "so:

- preverjanje skladnosti podatkov na dokumentaciji, pri bolniku in krvnih pripravkih ter potrditev z osebnim podpisom,
- neposredno prepoznavanje bolnika pred pričetkov transfuzije, informativno preverjanje podatkov o predhodnih transfuzijah, poteku, počutju in reakcijah,
- seznanjanje bolnika o trajanju transfuzije, z možnimi reakcijami in simptomi ter o načinu obveščanja medicinske sestre s klicno napravo,
- vstavitev venske kanile v skladu s strokovnimi navodili,
- nadziranje pretoka transfuzije- čas, pretok, i.v.kanila- prehodnost,
- opazovanje bolnika med potekom transfuzije na 30 minut ali manj po dogovoru,
- merjenje življenskih znakov na 30 minut ali manj po dogovoru,
- beleženje podatkov o bolniku v predpisano dokumentacijo,
- obveščanje zdravnika o pojavu reakcij in zapletov pri bolniku med transfuzijo,
- po potrebi izvajanje postopkov oživljanja v skladu s pristojnostmi po strokovnem standardu,
- pravilno rokovanje s transfuzijsko vrečko in sistemom v primeru reakcij po dogovoru
- izvajanje predpisanih higienskih postopkov in razvrščanje odpadkov po navodilih po končani transfuziji,
- opazovanje bolnika po transfuziji.

Medinske sestre in zdravstveni tehniki sodelujejo v negovalnem timu pri čemer lahko medicinska sestra prenese določene naloge na zdravstvenega tehnika, vendar le za tiste za katere je zdravstveni tehnik strokovno usposobljen.

Zdravstveni tehnik je odgovoren za merjenje bolnikovih življenskih znakov med potekom transfuzije, opazovanje bolnika in obveščanje v primeru spremembe bolnikovega zdravstvenega stanja ter beleženje postopkov.

V postopkih ravnanja s krvjo je za prenos krvnih vzorcev na ZTM in za prenos krvnih doz iz ZTM , v skladu s strokovnimi navodili po standardu zdravstvene nege in navodili medicinske sestre, pooblaščen kurir.

Pri prenosu biološkega materiala upošteva zahteve in uporablja predpisana sredstva.

## Sodelovanje medicinskih sester pri zdravljenju s krvjo

Razvoj raziskovalnih metod v transfuzijski medicini, uvajanje novih metod dela in sprememb v klinični praksi, ki temelji na najsodobnejših dognanjih medicinske znanosti, velik razvoj laboratorijske medicine in razvoj zdravstvene nege, so v zadnjih petnajstih letih prispevali k varnejši transfuziji krvi.

K temu je velik delež prispeval tudi tehnološki razvoj, ki zagotavlja za bolnika in zdravstvene delavce varnejše in človeku prijaznejšo opremo in pripomočke. Za zagotavljanje varne transfuzije, preprečevanje možnih zapletov in izvajanje nadzora kakovosti zdravljenja s krvjo in krvnimi pripravki, so v zdravstvenem sistemu v veljavi zakonski regulativi in strokovni standardi, ki urejajo celotno strokovno področje preskrbe s krvjo.

## Standardni postopki zdravstvene nege pri ravnanju s krvjo

Standardi zdravstvene nege in strokovna navodila o postopkih zdravstvene nege v zvezi s transfuzijo krvi z upoštevanjem določil Zakona o preskrbi s krvjo, urejajo samostojno in sodelujočo vlogo medicinskih sestrer in zdravstvenih tehnikov in drugih sodelavcev. Namen je zagotoviti popolno varnost bolnika (tudi s strani zdravstvene nege) in tudi popolno zaščito medicinske sestre, ki v postopkih v zvezi s transfuzijo sodeluje

**Odvzem krvnega vzorca za določanje krvne skupine in navzkrižnega preskusa**

- prepoznava bolnika
- odvzem krvnega vzorca za določitev krvne skupine ali navzkrižnega preskusa
- označevanje vzorcev bolnikove krvi
- sodelovanje zdravnika in medicinske sestre pri določanju krvne skupine na diagnostični ploščici iz kapilarne in venske krvi.

**Naročanje krvi in krvnih pripravkov z naročilnico in po telefonu**

- naročanje krvi v rednem času
- nujno naročanje krvi
- naročanje krvi za načrtovane operativne posege
- naročanje krvi za avtologno transfuzijo krvi

**Prenos krvnih vzorcev na ZTM in prenos naročene krvi oziroma krvnih pripravkov iz ZTK do naročnika**

- priprava vzorca za transfuzijske preiskave
- prenos vzorcev krvi in naročilnic s kurirjem na ZTK
- prenos krvi in pripravkov iz ZTK na klinične oddelke
- prenos krvi in pripravkov v Enoto za hranjenje krvi in krvnih pripravkov v bolnišnici

- izdaja in prevzem krvi in pripravkov iz Enoto za hranjenje krvi in krvnih pripravkov v bolnišnici

**Shranjevanje krvi in krvnih pripravkov**

- shranjevanjenje krvi in krvnih pripravkov na bolniškem oddelku oz. operacijski sobi
- shranjevanje in izdajanje krvi in krvnih pripravkov iz bolnišničnega depoja po protokolu ZTM

**Vračanje neuporabljene krvi**

- v bolnišnični Depo in na ZTM

**Namestitev i.v. kanala in izvedba transfuzije krvi in krvnih pripravkov**

- priprava bolnika na transfuzijo – obveščenost in pisni pristanek na zdravljenje s krvjo
- izbira pripomočkov za dajanje krvi
- sodelovanje medicinske sestre in zdravnika pri določanju krvne skupine na diagnostični ploščici
- zagotavljanje varne in pravilne priprave krvi in krvnih pripravkov v skladu z navodili in z uporabo aparatur za hranjenje in gretje pripravkov
- sodelovanje medicinske sestre in zdravnika pri nastavitvi i.v. kanala in aplikaciji krvi in krvnih pripravkov

**Naloge medicinske sestre med prejemanjem krvi ali krvnih pripravkov in dajanju krvi in krvnih pripravkov**

- opazovanje bolnika med transfuzijo,
- prepoznavanje reakcij na transfuzijo,
- poročanje in dokumentiranje o spremembah bolnikovega zdravstvenega stanja oz. neugodnih zapletih

Naloge medicinske sestre v zvezi z zapleti ob transfuziji in ukrepanje v okviru pristojnosti

**Izpolnjevanje standarizirane dokumentacije o transfuzijah** v skladu s 33.členom Zakona o preskrbi s krvjo in Pravilnikom o organizaciji in delovanju zdravstvene nege v KC Ljubljana

Zagotavljanje varnega okolja –ravnanje z odpadki, **Odredba o ravnanju z infektivnimi odpadki, ki nastajajo pri opravljanju dejavnosti Ur. l. RS, Navodila o ravnanju z odpadki, ki nastajajo pri opravljanju zdravstvene dejavnosti št. 57/94, Pravilnik o ravnanju z odpadki št.30/95, št.84/ 98**

## Sklepne misli

Kljub temu, da imamo zakonska določila in predpisana strokovna pravila obstajajo v praksi zelo nejasna pooblastila in ni spoštovanja delitve del v zdravstvenem timu. Zdravniki zaradi "pomanjkanja časa " prepuščajo medicinskim sestram samostojno izvajanje transfuzije krvi in krvnih pripravkov. Zaradi premajhnega števila zaposlenih in strokovno ustrezno usposobljenih medicinskih sester ter prevelikih delovnih obremenitev ob bolniku, se prenašajo pooblastila za izvedbo postopkov na nižje izobražene in ne dovolj usposobljene zaposlene. Posledice take prakse se kažejo v kazalcih uspešnosti zdravljenja.

Medicinske sestre pričakujemo, da bo uvedba standardov in Bolnišničnih transfuzijskih odborov, pripomogla k izboljševanju strokovnega dela in delovnih pogojev ter zmanjševanju nenapisanih pravil obstoječe prakse. Skrb za varnost bolnika ne more biti zgolj na papirju, sledenje napak in poročanje o neželenih dogodkih mora postati delovna obveza vseh, ki sodelujejo pri procesu zdravljenja.

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# Odgovornost zdravnika in višje medicinske sestre pri transfuziji krvi

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## Uvod

Čedalje več je mednarodnih konvencij, deklaracij in smernic, ki urejajo najrazličnejša medicinska področja. Ta področja so nato urejena še s pravnimi predpisi posamične države ter z etičnimi in deontološkimi kodeksnimi priporočili in določili. Postopke v zvezi s transfuzijo opredeljuje Etični kodeks o transfuziji, ki ga je leta 1980 sprejelo mednarodno združenje za transfuzijo krvi, v katerem so v obliki pravilnika uredili odnose do krvodajalca, do prejemnika krvi ter preverjanje ali transfuzijske ustanove upoštevajo mednarodna merila in če so njihovi pravilniki skladni s citiranim kodeksom. Vse elemente kodeksa je povzela tudi zakonodaja naše države v Zakonu o preskrbi s krvjo, ki je bil sprejet v letu 2000 in stopil v veljavo sredi junija letošnjega leta. Oba dokumenta, tako zakon kot kodeks natančno določata vse pravice in dolžnosti vseh povezanih v verigi dejavnosti transfuzije krvi.

## Razpravljanje

Če si podrobneje ogledamo kodeksna določila Etičnega kodeksa o transfuziji krvi, le-ta za krvodajalca upošteva prostovoljnost, splošno informiranost, anonimnost, za zdravnika pa odgovornost za odvzem, preizkušanje krvi; vse to z namenom, da bi bili odvzemi za krvodajalca čim bolj varni in da prejemnik ne bi utrpel škode. Kodeks zahteva predvsem od zdravnikov, da ne dopuščajo zlorab in razsipavanja uporabe krvi pri transfuziji. Kodeks nato v točkah natančno razčlenjuje vse postopke na ravni krvodajalca, prejemnika ter kontrole oziroma preverjanja vseh postopkov.

Novi moment je nastopil s sprejetjem Zakona o preskrbi s krvjo, ki natančno in decidirano opredeljuje zdravnikovo pojasnilno dolžnost napram krvodajalcu ter pridobiti krvodajalčevo pisno potrditev za njegovo prostovoljno sodelovanje. Kot vidimo, je krvodajalec po novem zakonu nekako povsem izenačen s pacientom in njegovimi pravicami v procesu zdravljenja, čeprav kot tak ni bolnik oz. subjekt v procesu zdravljenja.

Zdravnikova pojasnilna dolžnost ter "preiskovančeva" (darovalčeva) prostovoljna privolitev sta torej osnovna elementa, na katerima je na preizkušnji tako zdravnik, kakor tudi medicinsko osebje, ki sodeluje v procesu transfuzije krvi. V tem segmentu se srečujemo lahko ne samo z etičnimi kršitvami, temveč tudi z zdravniško kazensko in materialno odgovornostjo.

Identična je zakonska zahteva do bolnika, ki bo prejemnik krvi in s pisno potrditvijo izjavi, da je bil predhodno natančno obveščen o transfuziji in vseh njenih posledicah ter da je v transfuzijo prostovoljno privolil. To je sicer bolnikova osnovna zakonska pravica, ki pa napram zdravniku ali drugemu zdravstvenemu delavcu pomeni zahtevno obligacijsko razmerje.

V zakonu so natančno opredeljena vsa določila, ki jih mora upoštevati transfuzijska medicina skupaj s kontrolo kvalitete in so več ali manj razumljiva ter jasno definirana. Odmik od predpisanega predstavlja pravno kršitev, ki ima za posledico tudi etično odgovornost.

V kazenskih sankcijah je predpisana denarna kazen za vse kršitve navedenega zakona. Ali morda v ravnanju zdravnika ali višje medicinske sestre vidimo tudi kazensko odgovornost v smislu storitvenega ali opustitvenega dejanja Kazenskega zakonika R Slovenije? Vsekakor lahko odgovorimo pritrdilno. V procesu zdravljenja in prejemanja krvi velja predvsem "storitveni" element kaznivega dejanja in sicer, če v procesu zdravljenja zdravnik ali drug zdravstveni delavec nekaj stori, da se bolniku poslabša zdravje ali celo nastopi smrt, so izpolnjeni kriteriji strokovne napake in sicer kriteriji, ki opredeljujejo kaznivo strokovno napako. Ti kriteriji so predvsem trije in sicer:

1. malomarnost,
2. hudo neznanje,
3. namernost

Malomarnost lahko iščemo pri celotnem, natančno predpisanem postopku na vseh ravneh in jo je potrebno posebej dokazovati. Tudi drugi element kaznive strokovne napake je podobnega izvora, medtem ko tretji element, to je element "namernosti" izredno težko dokazujemo in se po navadi prekrije s prvim elementom. Tudi v pravni praksi je ta element bolj naveden kot teoretična možnost, ki je v praksi izjemna.

## Vprašanja ob bolnikovi odklonitvi transfuzije kljub medicinski indikaciji

Pri zdravljenju nekaterih skupin bolnikov včasih naletimo na odklanjanje transfuzije krvi iz ideoloških razlogov. Odklonitev transfuzije krvi spada v eno izmed zakonskih pravic bolnika po Zakonu o zdravstveni dejavnosti R Slovenije, kjer bolnik lahko delno ali v celoti odkloni predlagano terapijo. To svojo pravico hočejo uveljavljati še posebej tisti bolniki, ki so pripadniki nekaterih skupnosti, kot na primer Jehove priče ter pripadniki nekaterih, v Sloveniji sicer maloštevilnih eksotičnih sekt. Zdravstveni delavci smo v zvezi s transfuzijo dolžni spoštovati njihove želje in jim natančno razložiti in utemeljiti potrebo po prejemu krvi ali krvnih derivatov za morebitno reševanje njihovega življenja. Po drugi strani pa se moramo zavedati, da je naša osnovna dolžnost varovati in reševati življenje in da v vseh urgentnih zadevah nobena ideologija ne more biti nad pravnimi predpisi ter doktrinarnimi načeli.

Problematika v zvezi s transfuzijo ter nekaterimi drugimi sorodnimi posegi se danes označuje kot "komercializacija človeškega telesa in njegovih delov". Medicinsko in "industrijsko" ravnanje s substancami človeškega telesa postavlja številna vprašanja, pri čemer naj omenimo predvsem problematiko varstva človeškega telesa , lastnine in osebnosti. Pri krvodajalstvu kot "človekoljubni dejavnosti, ki se izvaja v skladu z načeli prostovoljnosti, brezplačnosti in anonimnosti" je posebej poudarjeno "darovanje – donorstvo" za določeno uporabo. Z vidika civilnega prava se nam dandanes postavlja vprašanje lastnine človeškega telesa. Pravica človeka na svojem telesu je osebnostna pravica. Veliko bolj zapleteno pa je vprašanje glede delov (tudi krvi ali krvne plazme) človeškega telesa po ločitvi. Po konvencionalnem civilnopravnem pojmovanju gre v tem primeru za "stvar", človek pa se označuje kot "lastnik". Omenjeno se označuje kot prehod osebnostne kvalitete v stvarno, s tem pa preusmeritev iz osebnostne k stvarni pravici. V tem se zrcalijo tudi materialni interesi zaradi razpolaganju oziroma dajanju telesnih substanc v promet. Prav v tem segmentu v krvodajalstvu daje odločilni moment prostovoljno krvodajalstvo na osnovi donorstva.

## Zaključek

Navrgli smo le nekaj etičnih dilem ter vprašanj, s katerimi se srečuje tako zdravnik kakor tudi drug zdravstveni delavec pri transfuziji krvi, ki je postavljena v sodobne pravne okvirje, vendar kljub temu lahko predstavlja določene pasti in zmote, ki imajo za posledico tako kazensko, kot moralno in odškodninsko odgovornost.

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# Tveganje in varnost kirurškega posega

*Arnež Z.*

Ob vstopu v tretje tisočletje kirurški bolniki upravičeno pričakujejo, da bodo rezultati kirurškega zdravljenja ugodni, da bodo izboljšali funkcijo in čim manj prizadeli videz.

Povpračevanje po kirurških posegih raste, pričakovanja bolnikov so vse večja, napredek stroke v kirurgiji, anesteziologiji in intenzivni medicini pa omogoča kirurške posege pri bolnikih, ki smo jim včasih odsvetovali operacije zaradi prevelikega tveganja.

Odločitve o tem kdaj, kje, kako in na katerih bolnikih naj se izvajajo kirurški posegi morajo biti logične pri čemer naj prva skrb velja varnosti bolnika.

## 1. Nujni posegi

Kirurg je pogosto prvi zdravnik, ki zdravi poškodovanca, zato bolnikov ne more izbirati. Največkrat pa je le eden izmed članov skupine zdravnikov in negovalnega osebja, ki timsko, multidisciplinarno obravnava bolnika, še posebej kadar gre za politravmo.

Upoštevaje etiologijo in težo poškodb mora odločiti o tem, ali bo kirurški poseg potreben takoj (urgentni kirurški poseg), ali ga je mogoče ali celo potrebno odložiti (odložen kirurški poseg).

Odločitev temelji na:

- **ugotovitkih splošnega stanja bolnika in njegove prognoze**, do katerih pride po natančni anamnezi in fizikalni preiskavi ter dodatnih diagnostičnih posegih (RTG,UZ, CT, NMR, EKG, laboratorij).

  Kadar je bolnikovo stanje slabo, lahko oskrba nepomembnih laceracij na obrazu ali udih brez težav počaka. Prioriteta v takih primerih je namenjena oskrbi poškodb ali stanj, ki ogrožajo življenje.

- **teži in lokalizaciji poškodb, ki obrožajo življenje**

  če se splošno stanje po zaustavitvi krvavitev v trebuhu, prsnem košu in glavi stabilizira, je varno oskrbeti še druge poškodbe (npr. odprti zlomi), če oskrba ne pomeni dodatne nevarnosti za bolnika.

- **času, ki je minil od poškodbe (nastanka stanja) do takrat, ko lahko zagotovimo varno in učinkovito kirurško zdravljenje**

  Kadar je od poškodbe minilo več ur in ugotavljamo prepričljive znake okužbe, poškodba pa nezahteva takojšnjega kirurškega posega, je za bolnika varneje, da kirurško oskrbo odložimo.

  Kirurško tveganje je pri urgentnih kirurških posegih pri življenje ogrožujočih stanjih, posebej pri sočasni prizadetosti večih organskih sitemov (npr. pri politravmi) največje.

  Zahteva hitro in učinkovito prvo pomoč, hitro predoperativno diagnostiko in pripravo, stalno dostopnost krvi in krvnih pripravkov (depo), dobro anestezijo, prisotnost izkučenega multidisciplinarnega kirurškega tima, ki je sposoben rešiti vse kirurške probleme in učinkovito intenzivno pooperativno zdravljenje.

## 2. Načrtovani posegi (npr. rekonstrukcijska kirurgija)

Rekonstrukcijska kirurgija popravlja izgled in funkcijo po prirojenih anomalijah, poškodbah ali tumorjih.

Izbira bolnikov temelji na:

- **bolnikovih ciljih, željah in prognozi**

  Rekonstrukcijo dojke opravimo vsem bolnicam, ki to želijo, ne glede na prognozo, seveda, še so sposobne za operativni poseg brez tveganja. Če pa imajo zasevke v kosteh in jetrih ter srčno popuščanje, je kirurško tveganje preveliko in jim operacijo odsvetujemo.

- **realnih pričakovanjih svojcev**

  Nedonošenček se rodi z encefalokelo na korenu nosu. Starši zahtevajo takojšen kirurški poseg. Najprej je potrebna diagnostika (CT, NMR) in ureditev splošnega stanja, šele nato ledi poseg po strokovnih merilih.

- **kirurgovi presoji**

  Presoditi mora ali je možnost dobrega rezultata večja od nevarnosti zapletov, še posebej kadar gre za že prej večkrat operiranega bolnika. Prisotnost prejšnjih brazgotin in slabe prekrvljenosti tkiv zaradi obsevanja močno povečuje možnost zapletov.

- **kirurgovih tehničnih zmožnostih**

  Kirug se mora vprašati ali lahko npr, pri mikrokirurškem posegu zagotovi bolniku enako ali podobno verjetnost uspeha kot drugi kirurgi. Kadar je odgovor ne, mora bolnika poslati k kolegom, ki sodegajo boljše rezultate na tem področju.

Estetska kirurgija

- ali obstajajo kontraindikacije za kirurški poseg
- ali bolnik/ca realno gleda na pričakovan rezultat kirurškega zdravljenja
- ali kažejo bolniki znake psiholoških ali emocionalnih težav, ki bi lahko vplivale na normalen pooperativni potek
- ali si kirurški poseg želi bolnik ali njegova okolica
- ali lahko kirurg s svojim znanjem ustreže bolnikovim željam
- razmerje med deformiteto in zaskrbljenostjo (Gorney)

Tveganje je preveliko, če obstaja velika zaskrbljenost ob majhni deformiteti.

## Izbira bolnikov

Na kirurško tveganje vplivajo številne bolezni in stanja.

1. **Nekirurške bolezni in stanja**

1. **Starost**

   Boniki na začetku in koncu starostne lestvice tvegajo več kirurških zapletov ali celo smrt ker imajo ožje območje kirurške varnosti. Manjše napake, ki jih mlad odrasel človek zlahka prenese, imajo pri dojenčkih ali strarostnikih (starejših od 80 let) lahko katastrofalne posledice.

1.1. **otroci**

1.1. 1. Že majhne izgube krvi ali tekočine lahko povzroče hudo hipovolemijo.

1.1.2. Pomanjkanje K vitamina pri novorojencih lahko povzroči hipoprotrombinemijo in posledično krvavitev.

1.1.3. Vročina lahko povzroči konvulzije ali kolaps žilja. Načrtovane operacije zaradi vročine odložimo.

1.2. **starejši (nad 80 let)**

1.2.1. Operativno tveganje ocenjujemo po fiziološki in ne po kronološki starosti. Starost sama po sebi ne sme biti razlog za odklanjanje operativnega posega. Tveganje po 60 letu starosti se poveča na račun srčno-žilnih, ledvičnih ali drugih resnih sistemskih bolezni.

1.2.2. Za vsakega bolnika, ki je starejši od 60 let moramo tudi kadar nima znakov, sumiti da ima generalizirano aterosklerozo in zmanjšano srčno in ledvično rezervo. Zato morajo biti preiskave pred operacijo zelo široke.

1.2.3. Neodkrit rak je pri tej starosti dokaj pogost, zato je potrebno preveriti prebavne in druge težave, čeprav se zdijo nepomembne.

1.2.4. Pri preobremenitvi cirkulacije s tekočino pri starostnikih rado pride do srčnega popuščanja. Pozorno je treba nadzorovati vnašanje, izločanje, telesno težo, vitalne znake ter serumske elektrolite.

1.2.5. Starostniki potrebujejo nižje odmerke narkotikov, pomirjevalin anestetikov kot mlajši bolniki. Narkotiki lahko povzroče depresijo dihanja, barbiturati pa zmedenost.

2. Debelost

Debeli bolniki imajo več resnih spremljajočih bolezni ter več zapletov s celjenjem rane in trombembolijami. Debelost tudi tehnično otežuje kiruški poseg in anestezijo. Zato je včasih priporočljivo odložiti elektivne operativne posege dokler bolnik z ustrezno dieto ne izgubi odvečne teže.

3. Imunska pomanjkljivost

O imunski pomanjkljivosti govorimo kadar je bolnikova sposobnost da ustrezno odgovori na okužbo ali poškodbo zmanjšana zaradi vpliva bolezni ali povzročitelja.

Glavna problema pri takih bolnikih sta veča dovzetnost za okužbo in počasno celjenje rane.

Večja dovzetnost za okužbo nastane zaradi :

a) zdravil (kortikosteroidi, imunosupresijska zdravila, citotoksična zdravila, dolgotrajno zdravljenje z antibiotiki)
b) podhranjenosti
c) renalne odpovedi
d) granulocitopenije in bolezni, ki povzročajo imunsko pomankljivost (limfomi, levkemije, hipogamaglobulinemije)
e) nekontroliran diabetes

4. Alergije in občutljivosti

Zabeležiti je treba vse neobičajne reakcije po injekciji ali zaužitju naštetih snovi, ki se jim nato moramo izogibati :

a) penicilin ali drugi antibiotiki in sulfonamidi
b) narkotiki
c) aspirin in drugi analgetiki
d) prokain in drugi anestetiki
e) barbiturati
f) tetanus antitoksin in drugi serumi
g) jod in drugi antiseptiki
h) katerekoli preveze
i) hrana
j) lepilni takovi

5. Sedanja zdravila

Zdravila, ki jih bolnik pravkar jemlje je potrebno bodisi ukiniti, bodisi nadaljevati z jemanjem ali pa prilagoditi odmerke. Nadaljevati je potrebno z digitalisom, insulinom in kortizonom, odmerke pa skrbno prilagajati med operacijo in v pooperativnem obdobju. Posebej skrbno je potrebno nadzorovati ali celo ukiniti antikoagulantna zdravila.

## 2. Bolezni srca in ožilja

Kiruški poseg in anestezija obremenita normalni srčno-žilni sistem v odvisnosti od :

1. velikosti, lokacije in tipa posega
2. trajanja posega in anestezije
3. okoliščin med operacijo (urgentna, elektivna)
4. drugih posledic operativnega posega (izguba in nadomeščanje krvi, ekstremne spremembe krvnega tlaka in frekvence, hipotermija, premiki tekočin med intravaskularnim in intersticijskim prostorom).

Vse našteto poveča potrebo srčne mišice po kisiku in zmanjša njeno preskrbo s kisikom. Take spremembe bolnik z normalnim srčno-žilnim sistemom zlahka prenese, medtem ko bolnika z organsko srčno boleznijo hudo prizadenejo.

**Kazalci srčnega tveganja pri kirurških posegih, ki niso povezani s srčno-žilnimi operacijami**

- diagnoza tretjega srčnega tona pred operacijo ali dvig jugularnega venskega tlaka
- prebolel akutni miokardni infarkt v prejšnjih 6 mesecih
- več kot 5 prezgodnjih miokardnih kontrakcij (PVC) na minuto
- prisotnost ne-sinusnega ritma ali prezgodnjih atrijskih kontrakcij (PAC) na preoperativnem elektrokardiogramu
- starost več kot 70 let
- prejšnji kirurški posegi v trebuhu, prsnem košu ali na aorti
- urgentni kirurški poseg
- padec sistoličnega krvnega tlaka med operacijo za 33%, ki traja več kot 10 minut
- pomembna stenoza aortne zaklopke

Taki bolniki potrebujejo natančno obdelavo pred operacijo v kateri naj sodelujejo osebni zdravnik, anesteziolog, kardiolog in kirurg.

Povprečna mortaliteta pri srčnih bolnikih po abdominalnih ali torakalnih operacijah je 3%. Seveda pa je pri določenih srčnih boleznih tveganje večje (npr, koronarna bolezen).

Kirurško tveganje (mortaliteto) podvoji srčno popuščanje ali angina pectoris ob majhnem naporu. Tveganje je še večje pri hudih aritmijah ali kadar je bolnik v zadnjih 6 mesecih preživel infarkt.

Angina pectoris v mirovanju štirikat poveča tveganje. Pravkar preboleli miokardni infarkt tveganje tako poveča, da predstavlja kontraindikacijo za operativni poseg.

## 3. Pljučne bolezni

Akutne in kronične pljučne bolezni večajo operativno morbiditeto in mortaliteto.

Potrebna obdelava bolnika pred operacijo je odvisna od njegove starosti, prejšnjih bolezni in vrste načrtovane operacije. Za operacije v lokalni anesteziji taka obdelava ni potrebna.

Pred operacijo v splošni anesteziji pri bolnikih s kronično pljučno boleznijo starih več kot 60 let je potrebno določiti vitalno kapaciteto in FEV (forced expiratory volume) ter plinsko analizo arterijske krvi. Tveganje je največje pri bolnikih pri katerih bo potrebna torakotomija, še posebej kadar je načrtovana resekcija pljuč. Pri takih je potreben popoln pregled pljučne funkcije.

Akutna infekcija dihal (angina, faringitis, pljučnica) je kontraindikacija za elektivni operativni poseg. Tega lahko opravimo šele teden do dva tedna po koncu zdravljenja.

Kadar je operacija nujna, se izogibamo uporabi inhalacijskih anestetikov in sočasno pričnemo z zdravljenjem z antibiotiki (kadar sumimo, da gre za bakterijsko okužbo).

Kronične pljučne bolezni (kronični bronhitis, bronhiektazije, emfizem, astma) predstavljajo precejšnje tveganje za bolnika. Povezane so z obstrukcijo dihalnih poti.

Kajenje, ki spremlja te bolezni je že samo po sebi faktor tveganja. Bolniki morajo prenehati kaditi vsaj 14 dni pred načrtovanim kirurškim posegom.

Kronične pljučne bolnike je pred načrtovanimi operacijami potrebno natančno diagnostično obdelati.

## 4. Bolezni ledvic

Pred operacijo je potrebno skrbno oceniti funkcijo ledvic.

- Urediti je treba elektrolitske motnje. Pri hudi odpovedi ledvic je potrebna hemodializa.
- Ledvični bolniki imajo pogosto anemijo. Adaptirajo se na hematokrit okoli 20% in potrebujejo transfuzijo le ob večji izgubi krvi. Transfuzija mora biti previdna, da se izognemo srčni dekompenzaciji.
- Pogoste so krvavitve zaradi disfunkcije trombocitov. Elektivni kirurški posegi morajo počakati dokler se s hemodializo ne vzpostavi funkcija trombocitov.
- Zdravila proti hipertenziji je potrebno pred operacijo prekiniti. Vedeti pa je treba, da ukinitev klonidina lahko povzroči paroksizmalno hipertenzijo, propanolola pa srčne aritmije.
- Izogibati se je potrebno nefrotoksičnih zdravil in tudi odmerke antibiotikov prilagoditi zmanjšani ledvični funkciji.

## 5. Motnje hemostaze

Najbolj pomembno je, da pred operacijo, kadar je le mogoče, natančno določimo za kakšno motnjo koagulacije ali hemostaze gre. Nato ustrezno ukrepamo.

## 6. Endokrine motnje

6.1. Diabetes mellitus

Nadzorovan diabetes sam po sebi ne povečuje operativnega tveganja. Res pa je, da so diabetiki fiziološko 8 do 10 let starejši kot kaže kronološka starost in da pri njih ateroskleroza nastane prej.

Če hočemo zmanjšati mogoče srčne, žilne, ledvične in možganske zaplete, moramo uporabiti čim lažjo anestezijo in bolnika čim prej spraviti pokonci. Predvsem je treba pozornost polagati na večjo verjetnost okužbe in se odločiti za perioperativno uporabo antibiotikov. Nujno je vzdrževati euglikemično stanje.

6.2. Bolnik, ki se zdravi s kortikosteroidi

Gre tako za bolnike, ki so kdajkoli prejemali glukokortikoidie kot za tiste, ki jih še prejemajo. Pri takih bolnikih vseskozi obstaja, v odsotnosti podporne terapije s kortikosteroidi, nevarnost pooperativne adrenalne insuficience in šoka.

4.3. Hipotiroidizem

Kadar je le mogoče je potrebno pred načrtovano operacijo povečati hitrost bazalnega metabolizma do skoraj normalne in s tem izboljšati celjenje ran ter srčno in pljučno funkcijo. Številni bolniki s hipotiroidizmom imajo angino pectoris, tako da lahko prehitro dodajanje ščitničnega hormona povzroči infarkt.

## 7. Nosečnost

Akutne operacije pri nosečnicah je treba opraviti takoj, elektivne posege, ki ne ogrožajo zdravja pa je varneje odložiti na čas po porodu.

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