

Opinion on blood transfusion with reference to not making commercial use of the human body

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Opinion

The National Consultative Ethics Committee established its position on this issue in the presentation of the initial work of the Group "Ethics and money" :

"When it is said that the human body is not for sale and not on the market, the two statements are complementary : on the one hand, the human body or one of its components cannot be the object of a contract, one the other hand, it cannot be negotiated by anyone".

The Committee re-asserts this principle, which must apply to both the human body as a whole and to organs and components.

As regards blood donation and more generally the French transfusion system, the Committee reiterates its endorsement of the fundamental values which inspired the system :

- *voluntary unpaid donation*
- *non-profit for subsequent operations*
- *dignity of the donor*
- *interests of the patient.*

A reorganisation of structures is necessary but must continue to be based on these principles, and must also take into account all the objectives : safe collection and distribution of products, sober and reasonable economic use, capacity to finance research and investments. These principles entail total transparency and strict supervision of the use of funds for scientific work and for day to day operations.

Developments in European economic co-operation should not compromise these principles.

In this respect, a directive by the Council of European Communities, dated 14th June, 1989, which calls blood and human plasma " *raw materials* " and blood components "

pharmaceutical items " would seem to include these products of the body into the commercial circuit. This interpretation of the document should not take precedence over the principles recalled above.

Purchasing blood and plasma as one would buy a raw material and selling plasma derivatives, would be a negation of the above principles.

Any concession, on the pretext that blood is a renewable tissue and that limited donation cannot be harmful, would transgress the rule which ensures that human dignity is respected. Once blood has become a commercial item, all other tissues and organs could go the same way.

In Europe a major effort is in progress to bring nations closer together, in particular economically. The Council of Ministers of the Council of Europe, when it adopted recommendation n° R-90-9 of 29th March, 1990 which states " *for reasons both ethical and clinical, blood donation should be voluntary and should not give rise to remuneration* ", is in fact taking a different direction.

The National Consultative Ethics Committee thereby finds reason to declare that unification will not be achieved successfully, and therefore the ideal of arriving at harmonisation will not be attained, if solely economic interests are taken account of, without any reference to the ethical values which this Opinion reaffirms.

Report

Blood transfusion has been for a long time one of the National Consultative Ethics Committee's particular preoccupations ((1)*) . The subject has just sprung to the foreground of national concerns in dramatic circumstances. This report comes therefore at a time when there is coincidence between action based on a principle and the testing of that principle by current events.

Early in 1990, our Committee embarked on an in depth study on the theme of "Ethics and Money", the pertinence of which never ceases to be patent in most of the matters we are asked to consider. As a first step in this long term consideration of the matter, in the " *Journées Nationales d'Ethique* " in December 1990, the Committee re-affirmed the fundamental principle of not making commercial use of the human body. Since that time, work has progressed. One of the subjects which we feel we have completed our consideration of, and which will be one of the major components of the final report, is blood transfusion. As of now, it can be the subject of a report and a firm Opinion.

France played a leading role in the development of blood transfusion. The first transfusions, the first Transfusion Centre (Saint-Antoine, 1929), the first organised transfusion system on a national scale, all took place in our country. Furthermore, as early as 1950, the principle of unpaid blood donation was adopted and made the French system an internationally recognised ethical model.

And yet, that which seemed to have been established once and for all is challenged in a time of crisis, with consequences that may turn out to be very serious or perhaps irreparable.

There is a dual aspect to this crisis. The first, which has been the subject of much discussion and comment, is a loss of faith. The discovery that hundreds of haemophiliacs were contaminated by the AIDS virus at a time when effective decontamination of anti-haemophilic products had not become generalised, i.e. before mid-1985, provoked consternation with which we entirely sympathise. Queries, criticism, and doubts abound. Who bears responsibility or, in some cases blame, during this period ? Changes in outlook since that time, brought about by an enormous accumulation of recently acquired

knowledge, complicates the task of judging with hindsight and taking into account scientific uncertainties and technological hesitations of a period now past. The courts will have the task of throwing all possible light on this distressing issue, as devastated families and loved ones justifiably demand, and making whatever reparation they may be entitled to.

We have neither authority to intervene in such procedures, nor any inclination to do so.

The second aspect of the present crisis, less apparent perhaps to public opinion, is in fact of much greater scope and gravity. We refer to the fact that the principles of the system as a whole are questioned, and that these principles are viewed in an equivocal light although they are in no way involved in the calamitous events before 1985. Our mission does not qualify us to evaluate the failings of the system or of its structures, or their causes nor who is to be held responsible. But this mission definitely empowers us to make a firm ethical stand upholding those principles which are : absence of gain, and banning commercial use of the human body.

Changes which have been introduced in the last few years in the *Centre National pour la Transfusion Sanguine* (National Blood Transfusion Centre) could, if they were to persist, gravely imperil the ethical principles which are at the root of the remarkable and original qualities of the system as a whole.

These changes were brought about by revolutionary technical modifications to the process of blood transfusion. Traditionally, transfusion was a direct transfer of whole blood, but has now evolved so that elective use is made of the various components of blood and plasma, according to the patient's specific needs. In this way, processes of an almost industrial nature have appeared such as industrial extraction and preparation of stabilised products for therapeutic purposes. This dual evolution has led in some countries, the United States in particular, to a pharmaceutical statute for the institutions preparing the products. Industrial logic leads to a commercialisation of the whole process, blood is bought, and its components are sold, after preparation.

The risk of this kind of development in France is all the less negligible since the European arrangements which will become mandatory in 1993 move in that direction.

There is danger for the future of our system in both of its aspects : unpaid blood donation, and the non-lucrative character of subsequent activities.

We have entered into an era of industrial logic : that cannot be avoided. We are now threatened by commercial logic : is it avoidable ? This is the fundamental question we wish to broach after considering :

- developments in transfusion
- features of the French system
- European directives on blood and plasma, and their consequences.

1 - Developments in transfusion

The expression 'blood transfusion' now includes :

collection of whole blood or of plasma only (plasmapheresis)

separation of the blood components : on one hand, cellular components - red blood cells, white blood cells, and platelets; on the other hand, plasma derivatives obtained by fractionation

rejection of whole blood very rarely, usually only one or other of its components, depending on the patient's need.

The increasing complexity of transfusion techniques is due to technical progress and to new indications.

Technical progress

A bloodless human dies. This obvious fact led a very long time ago to the concept of transfusion. After very disappointing early attempts with animal blood, the use of human blood at the end of the 19th century raised hopes. They were frequently dashed, however, by inexplicable failures.

They remained unexplained until Landsteiner, in 1900, discovered that all human blood was not identical - neither identical nor, worse still, compatible. An essential breakthrough was the discovery of the first three human blood groups, A, O, B, which are the most important from the point of view of compatibility.

This decisive step forward and the needs engendered by World War I triggered early applications. At the time, transfusion was direct from arm to arm. After the war, various devices greatly facilitated the procedure.

In 1929, Arnault Tzanck, who had been one of the pioneers of the technique, founded the first blood transfusion centre in Paris, at the hospital Saint-Antoine. Physicians and donors were on standby around the clock so as to be able to respond to any emergency in all of the Paris hospitals. This was the first transfusion system.

World War II brought further progress : the preservation of blood. Blood could be stabilised and stored for several days for transport and used elsewhere, at a later time. Moreover, it could be checked biologically before use.

After the war, blood transfusion centres were established in the major hospitals. Some of them began to use separation techniques so that blood cells and plasma could be used separately.

This developed in response to an increase in demand, i.e. in indications.

Development of indications and industrialisation of plasmatic fractionation

Initially designed to correct a partial loss of blood volume, transfusion was in the beginning an injection of whole blood. The only indication at the time, haemorrhage, seemed to logically call for this kind of global compensation. However, progress in the technology of resuscitation during World War II, revealed that the most threatening characteristic of a haemorrhage is a collapse of circulation due to a drop in blood volume. The idea was born of replacing as a priority the missing volume with plasma only, if necessary. Plasma, once separated from blood cells can be easily stored and preserved. The advantage therefore is greater availability. Once blood volume has been restored, the loss of red blood cells has to be compensated, but it is then only necessary to inject cells in the concentrated form which is the result of fractionation. Thus, the concept of selective transfusion began to emerge in the 1960s.

In parallel, indications multiplied and ceased to be purely surgical. Clinical indications included correcting anemias, white blood cell and platelet deficiencies, or a lack of certain plasma components such as clotting factors.

In each of these cases, it seemed logical to inject only the missing component. Furthermore, selective transfusion saves blood. Various therapeutic products can be derived from the same blood donation.

The development of techniques for separating blood into cells and plasma and then isolating

the component proteins of plasma, a process which is called plasma fractionation, naturally ensued.

These separation techniques give rise to two kind of products :

cellular components (labile products) which cannot be stored for any great length of time : a few weeks for red blood cells, and only a few days for white blood cells and platelets.

plasmatic fractions, which are much more stable and can be stored for months or even years.

Equipment required for each of these two kinds of procedures varies considerably. Production of labile products does not require any very complex equipment. It can be done by most blood transfusion centres. Plasma fractionation, however, requires complex machinery. You could say that labile products can be prepared in an unsophisticated environment, processed and used in unit form, but with all the problems of verifying compatibility at the time they are used. On the contrary, stable products fall into the category of industrial processes in batches of several thousands of litres of plasma. These products are standardised and can be used by anyone following prescriptions for indications and general administrative procedures.

The development of plasma fractionation activities has led to the creation of industrial facilities processing plasma in gigantic quantities : several hundreds of thousands of litres a year.

Initially, plasma was the result of separation of the cell components from whole blood; it was a kind of "by-product" of the preparation of labile products by blood transfusion centres. But as the growth of demand for stable fractions outpaced the growth of demand for labile products, the result was selective collection. Certain machines can, during the collection of blood from a donor, separate the cellular components which are re-injected, and keep only the plasma. This is called plasmapheresis and allows for collection of larger and much more frequent donations than is the case with whole blood.

In this way, and particularly in certain countries, an independent plasma industry has evolved which closely resembles the pharmaceutical industry.

Developments in transfusion in other countries

We are not attempting to give an overall view of transfusion world wide. We simply wish to give an impression of the diversity that exists using a few examples which will help to understand the specificity and harmony of the French system which will be described below.

The United States are a special case for a variety of reasons. Firstly, because there are two types of transfusion centres, those run by the Red Cross, and others with widely differing statutes. Only the first category apply the ethical principles of non payment of donors, and non-profit for the centre. But the major specific characteristic of the country is the enormous development of a plasma industry run by a few large companies along commercial lines. They buy the plasma obtained by plasmapheresis and sell the fractions in the same way as medicinal drugs (they may also sell the non processed plasma as a " raw material " to fractionating centres, even in Europe as we shall see). As these companies are very dynamic they produce quantities far higher than are needed on the American home market (needs are evaluated at about 3 000 000 litres of plasma whereas about 9 000 000 litres are drawn). As a result, they export a great deal of their production at prices which on the whole are significantly lower than those practised by fractionating centres using donated plasma. This is because as "donors" are paid, conditions are imposed on them which ensure better productivity from the plasmapheresis machines and blood centre staff.

For a long time, Japan imported blood products from the United States for two reasons :

essentially because not enough blood was collected, but even more because consumption was excessive, particularly of plasmatic products. However, contamination of haemophiliacs by the AIDS virus at a time when the country was virtually free of sexual contamination, led to a radical change of policy.

Self-sufficiency based on voluntary donation and a slowing down of consumption is not far off, which is beginning to worry American exporters and incite them to turn their eyes in the direction of Europe.

European transfusion centres differ notably in the way they are organised and their degree of efficiency. The French system with centres as part of a public service exercising a monopoly is an exception. In certain countries, such as Belgium, Holland, and Denmark, the Red Cross is in charge of organising blood transfusion and sees to it that the rules of unpaid donation and absence of profit are respected. However, in certain countries, Germany in particular, paying the donor is not prohibited. Another particularity of the country, is that Germany consumes vast quantities of plasma, albumin, and antihemophilic factors, and therefore imports large volumes of American plasma (800 000 litres annually). Globally, Europe just about satisfies its domestic market for labile products. For plasmatic products however, it must import abundant quantities either as plasma, or as finished products.

Transfusion in the future

In France and in most countries with the same level of health care development, there is a levelling off of blood and blood product consumption. It would not be unreasonable to expect a downturn in the next few years. Several reasons may be involved.

Firstly, as a consequence of HIV contamination, there is increasing awareness of the risk of infection, viral infection in particular. Even when they are identified and can be detected, there is always a residual risk (at present, the risk of HIV transmission is estimated at 1 in 100.000 to 1 in 200.000 transfusions). But more menacing is the risk of new infections for which there is bound to be a lag before preventive measures are applied.

At first, only the medical profession was apprehensive about transfusion risks, but the general public is also becoming wary. Such fears are going to be the most powerful agents for reducing consumption which had reached in some cases excessive levels.

Apart from a more selective choice of indications, another trend is to find new methods to either replace blood with artificial substances (as we have seen previously, plasma substitutes to replace blood volume), or to use the patient's own blood for a transfusion instead of blood supplied by a donor. This is called *autologous donation* and is used in elective surgery when it is possible to predict some time in advance that transfusion will be needed.

Plasmatic fractions are likely to modify to the greatest extent the present situation. They are pure proteins, clearly identified and it is thought there could be hopes of creating them by genetic engineering. Two American firms have already manufactured a factor VIII which is out of the experimental stage and awaiting approval. The French National Transfusion Centre is also working on a factor VIII but is a little less advanced. Requirements for plasmatic factor VIII, which was the component which conditioned the level of plasma consumption, should take a sharp downward turn over the next few years. The same should apply to albumin which has been synthesised by several genetic engineering processes. Finally, another project of the National Transfusion Centre is to manufacture an anti-D immunoglobulin to be used clinically to prevent Rhesus immunisation.

Therefore, over the next decade, there should be a complete reversal of the situation regarding plasmatic proteins. However, the need for red blood cells, and even more for leukocytes and platelets are nowhere near to being satisfied by anything but blood donation.

2 - The French transfusion system

Particularities

The French transfusion system has some distinctive ethical and organisational features. After a short period of time after the war when donors received financial compensation, partly justified by the need to travel urgently demanded by the direct transfusion method, voluntary donation became the rule. Deferred transfusion made possible by techniques to preserve blood helped to achieve this, and also anonymity.

Donation free of charge introduced by the pioneers of transfusion, both medical staff and donors, later influenced the whole organisation of the transfusion system.

In 1952, a law was passed setting up the transfusion system which includes Departmental Centres (one for each *département* (French administrative areas), Regional Centres (a total of 16) and the National Centre which also takes on certain special tasks in education and research.

Some Regional Centres and, of course, the National Centre, have developed industrial activities for the fractionation of plasma (a total of 7 centres).

This system has the monopoly of collecting, preparing, and distributing blood and all its derivatives. As a logical follow-up to non lucrative donation, non profit making is mandatory. This is implemented through the setting of a "disposal" price (and not a sales price) for each of the products, by the government department in charge.

In this way, although the Centres do not all have the same legal status (some are hospital-based or community-based, and in some cases they are associations) but all together render a public service.

Another special feature of the French system is the role played by donors. They are members of associations which group together at national level to form the French Federation of Voluntary Blood Donors (Fédération Française des Donneurs de Sang Bénévoles). Donor associations at community level and the Federation at national level cooperate with blood transfusion establishments, specially for the purpose of promoting blood donation. The esteem and gratitude owed to the voluntary donor is apparent in the partnership statute conferred on him.

Evolution of the system

The system has had to adapt to the constant increase in demand.. It now collects approximately 4 million donations a year. This is entirely sufficient for labile products, and almost enough to satisfy demand for stable products. For the first time, in the last two years, fortunately limited quantities of plasma have had to be imported.

Adapting to the growth in demand has required efforts from all the Centres, and more particularly the fractionation Centres who in recent years have developed quasi industrial facilities to prepare the various fractions and process about 1 million litres of plasma a year. Yield efficiencies (extraction rate of the various proteins) have been improved constantly. The best performances are on a par with state of the art technology. It is worth noting that if all the fractionation Centres had attained that level, imports would not have been necessary in the last two years.

The National Blood Transfusion Centre has played a leading role in this evolution. Its educational activities in transfusion (most transfusion specialists are trained there), and research activities (work conducted by Professor Salmon enjoys international recognition) are worthy of note. The greatest effort however has been in the field of plasma fractionation and a powerful industrial tool is in the making.

Wishing to make the best use of this industrial capacity, the management have created in the past two years a joint stock company grouping a network of commercial subsidiaries, called *Espace Vie* .

The creation of *Espace Vie* has been described as necessary to adapt to pharmaceutical status developments which are said to be inevitable in the light of European regulations which will be studied below.

There is no denying, however, that creating a group of commercial subsidiaries could risk gravely tarnishing the altruistic image of the transfusion system. There is a potential source of flagrant contradiction of the non-profit principle of an organisation which must be entirely devoted to the sole interests of the patient and respect for the spirit of generosity of which the first example is set by donors.

Donor associations and quite a few physicians working in the transfusion centres did not entirely approve the move. Furthermore, excessive financial commitments compromised the economic balance of the National Centre.

The governmental authorities in charge of the Centres, became aware of the grave consequences of the move and are studying the matter in preparation for further action.

It is clear that the study must consider mainly the National Blood Transfusion Centre because of the change in its structures, but must also extend to a consideration of the whole French transfusion system particularly in the light of the implications of the European directive on blood and derivatives.

3 - The European directive on blood and its consequences

The Council of European Communities approved directive N° 89-381 on 14th June 1989, "setting up special arrangements for medication derived from human blood and plasma".

The essential point in this directive is that it confers the status of medicinal items to plasma derivatives. It hopes that States will achieve self-sufficiency using non paid donors, but it does not prohibit paid plasma from being imported, it does not demand non-profit status for the fractionation facilities which may be part of the private sector, and it provides for commercial distribution of the products.

The economic inspiration of this directive which aims to allow free circulation and production of "medication derived from human blood and plasma" outranks very clearly ethical considerations which take second place.

If the European Directive is implemented, there would be serious repercussions on:

- *ethics,*
- *the present transfusion system,*
- *public health,*
- *society.*

Ethical repercussions

Accepting the possibility of buying blood and plasma as a "raw material", and commercial sale of processed products, is above all, a denial of a fundamental principle of our legal system, i.e. refraining from making commercial use of the human body.

Quite recently, our Committee, when it presented the initial work of the Group "Ethics and money" recalled our attachment to this principle : *"When it is said that the human body is*

not for sale and not on the market, the two statements are complementary : on the one hand, the human body or one of its components cannot be the object of a contract, on the other hand, it cannot be negotiated by anyone".

Any concession, on the pretext that blood is a renewable tissue and that limited donation cannot be harmful, would transgress the rule which ensures that human dignity is respected. Once blood has become a commercial item, all other tissues and organs could go the same way.

We point out that our refusal should start with the rejection of wording such as "*raw material*" to designate blood and plasma, and "*medication*" to describe products prepared by processing blood and plasma.

The terminology, which is in itself alienating, opens the way to a deviation of concepts, principles, and practices.

However, in order to ensure maximum safety, it is advisable that all the guarantees which attach to the status of pharmaceutical items should be strictly applied to blood derivatives, which does not however confer on them the status of medication as such.

Consequences for the present transfusion system

The French transfusion system is based on a law passed in 1952 which set up a co-ordinated set of departmental, regional, and national Centres.

Together, they render a public service to which was given the monopoly for collecting blood, preparing derivatives, and distributing blood and components.

If the European Directive is implemented, this system will face threefold competition from the major commercial companies :

the companies could set up fractionation units in France,

they could buy plasma abroad, at a lower cost price than donated plasma,

they could, either through these units, or through their manufacturing facilities abroad, market lower priced products for two reasons. Firstly, because of the lower cost of the plasma, but also because they do not have to bear the cost of supplying the labile fractions. Commercial firms concentrate on the sole profitable side of the business, i.e. stable products. The labile sector is more difficult to manage and to run profitably. It would remain the responsibility of the national transfusion system, thereby increasing the deficit. But the most threatening outcome concerns voluntary donors who would cease to feel concerned if the principle of voluntary donation was dropped. They have made this sentiment known through their associations.

Altogether, the entire transfusion system as it is today would very soon be endangered and made incapable of performing a task which is essential for public health.

A reorganisation of structures is necessary but must continue to be based on a renewed assertion of ethical principles, and must also take into account all the objectives : safe collection and distribution of products, sober and reasonable economic use, capacity to finance research and investments. These principles entail total transparency and strict supervision of the use of funds for scientific work and for day to day operations.

Consequences for public health

Accepting that blood and plasma can be bought has further detrimental consequences for public health. It is obvious that in such transactions, there is a tendency to overstep the limits for volumes drawn which have been the rule for the sake of the donor's health. Both the collecting agency and the donor may be responsible for such abuses.

Also, the purchase of blood increases possible risks of contamination either by infectious agents, or by drugs, in two ways : there is a higher representation of the more deprived sectors of the population who are more exposed to risks of contamination of various kinds, and vendors are more likely to conceal risk factors.

Finally, in a system entirely governed by the law of the market, consumption might be encouraged even for marginal or aberrant indications. On the contrary, the unpaid character of the donation obliges collection and distribution agents not just to respect the non-profitable nature of the operation, but also sober and reasonable use, with a verification of indications, and a limitation, insofar as is possible, of the consumption of blood products which can be of immense therapeutic benefit, but nevertheless is not devoid of serious risk.

We recognise that the European Directive, by demanding therapeutic drug status which implies safeguards, and in particular checks and trials before a product is put on the market, seeks to give maximum protection. However, as we have already stated, it should be possible to demand identical safeguards without giving medication status.

Social consequences

A free gift is part of a social concept of solidarity which is all the more unselfish because the gift is anonymous. The collecting agency, responsible for non-profitability and conscientious use, is the public medium for this notion of mutual help and the recipient is aware of the priceless value of what he has been given.

In this way, the transfusion system, as it was designed in France, is a creator of social bonds. A "market" system cannot be expected to produce such wholesome results. On the contrary, it would create inequalities and in particular incite preferential removal of substance from the more deprived section of the population.

The European Directive appears to be inspired above all by economic considerations to promote free trade within the Community, but brings with it, in exchange for very limited safeguarding improvements, so many risks for the purity of the ethical principles involved and the potency of our transfusion system that one may legitimately wonder whether it is compatible with ethical principles which are reasserted above.

This questioning of the medication status could for that matter be to some extent justified by a similar trend in the United States, although for very different motives. At the request of the commercial companies themselves, the medication status is about to be dropped. The reason is that the status implies a degree of security which cannot now, and probably not in the future, be totally guaranteed. Thus, liability for risks which are difficult to foresee and estimate are becoming increasingly troublesome to insure. For those reasons, in the United States the notion of "service" is reinstated for transfusion, implying for the manufacturer simply an obligation to use adequate means and approved practices.

It would be paradoxical if Europe were to adopt a solution which is contrary to its ethical principles and which even in purely economic terms, is highly risky.

Notes

1.(*) see Opinion of 13th May 1985.