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Review article

Blood, perceptions, resource and ownership: When transfusion illustrates the complexity

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ABSTRACT

Blood is apart from the rest of the tissues as this fluid is overseen by basic and applied life and humanistic sciences. Blood is the essence of human functioning. It is the object of one of the most commonly known cancers, leukemia. It is life-saving in transfusion – a property that also gives blood a special credit and questions blood as a valuable merchandise or as no ones' property but common good. But blood is also scandalous after the tainted blood affair in the 1980s and 1990s. Blood is further inseparable from most religious practices, both forefront and hidden (magic cults). It is frightening as it is versed in legitimate and illegitimate combats; it is poured to compensate offenses or debts in many civilizations. Any time blood comes forefront, rationale science leaves it to irrational digressions. Even the very same life-saving transfusion, is beaten by groups of opponents on religious grounds. Further, at a time blood cells and molecules are scrutinized, no one can claim having a complete understanding of what blood is, off the vasculature, as – to study it – one has to alter it. The study of blood is fascinating for all colleges of an academy and not many topics can share this property: chemists, physicists, geneticists, physiologists, medical doctors, philosophers, ethicists, theologians, artists, historicists, anthropologists, sociologists, etc. have all contributed to depict different, specific, aspects of blood. The present review aims at merging different aspects of blood to give pathophysiologists a platform to better understand fears and hopes related to this special tissue, when dealing with patients of theirs.

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R É S U M É

Le sang est à part des autres tissus en ce sens que son étude relève tout autant des sciences fondamentales et appliquées que des sciences humaines. Le sang est au carrefour du métabolisme chez l'homme. Il est la cible d'un des cancers les plus connus et redoutés, les leucémies. Il sauve au travers de la transfusion, une qualité qui confère au sang une aura particulière, mais aussi qui ouvre la porte aux questions sur son identité en tant que bien (possiblement marchand) ou en tant que bien public. Le sang a été associé à un scandale sanitaire dans les années 1980 à 1990. Le sang est inséparable de la plupart des religions et pratiques religieuses, tant sur le devant de la scène que de façon occulte dans les rites magiques. Il est source de frayeurs quand il est versé dans les combats, légitimes ou illégitimes ; il est aussi versé en compensation de dettes d'honneur dans de nombreuses civilisations. Chaque fois qu'il est question de sang, l'aspect rationnel et scientifique peut laisser le champ aux digressions irrationnelles. Et c'est aussi le cas pour la transfusion salvatrice de vies qui trouve des groupes de personnes qui s'y opposent sur des bases religieuses. De plus, alors que l'intimité du sang est scrutée sur les plans cellulaires et moléculaires, on ne connaît pas le sang dans son entité essentielle, le sang qui circule en contact avec les vaisseaux, car pour l'étudier, on le modifie. L'étude du sang fascine tous les collègues du monde académique : chimistes,

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physiciens, généticiens, physiologistes, médecins, philosophes, éthiciens, théologiens, artistes, historiens, anthropologues sociologues, etc. ont tous contribué à illustrer et décrire certains aspects particuliers ou spécifiques du sang. Cette revue ambitionne de faire converger un certain nombre de ces aspects, afin de fournir aux physiopathologistes une nouvelle plateforme de connaissances et les aider à mieux appréhender les espoirs et les peurs inhérentes aux victimes de maladies du sang et leurs proches.

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1. Introduction

Blood is considered special among the rest of tissues, especially as it comes into several visible forms: liquid and red under its oxygenated arterial form; liquid and dark under its venous and also the menstrual form; solid and dark after a few minutes as a clot after wounding. Of interesting note, the so-called “physiological” blood is basically unknown even by blood specialists, because accessed blood is modified by the activation of clotting or anticlotting factors: genuine blood is in vessels only, unmodified; once accessed, it is artificially altered. Such oscillations in representations of the same tissue have fueled imagination: it is associated with god-centered fears and cults, and with man-centered philosophies (and – later – ethical debates) [1]. Oscillations in representations concern both religious and secular aspects, that comprises – in particular – blood transfusion [2,3]. Blood is indeed largely exchangeable within humans: initially restricted to humanitarian assistance through an arm-to-arm operation, transfusion has become more organized and, hundred years after its large-scale application, it now flirts with industrial processes [4]. Benevolence of blood donation and trade applied to plasma derivatives both have the same object, blood; whereas it is purely material in the latter, it may be both material and immaterial in the former [5]. This essay attempts to critically discuss some of those aspects.

2. Blood: life, death and justice

It is estimated that our prehistoric ancestors perceived that abundant spills of blood lead to death, especially when caused by weapons (as shown on painted caves such as Altamira, Spain). Then, severe perinatal hemorrhage was not an uncommon cause of fatalities over ages, long attributed to females’ fragility, or a fatalist inability to survive (“That’s life”). When medicine became forensic, pathophysiology made progress and a number of pathological states were discovered, such as leukemias. Leukemia affects children occasionally and such occurrences are strikingly overseen as global injustice. This emphasized some bad reputation credited to blood, until leukemias became largely curable especially in the youth, and transfusion of blood components of which platelets gained virtue as saving partners of chemo- and radio-therapy [6]. In an oscillatory manner, blood regained bad reputation when infections were transmitted, reemphasizing a sense of injustice: the first sentence was the disease, the second one was chemotherapy and consequences (i.e. the loss of fertility, etc.), and the third one was transfusion associated infection [7]. It took near two decades to reverse this representation, though only partially according to peoples’ representations.

3. Blood spills: from war to entertainment

Historic narrations report on the importance of seeing blood versed by enemies. Combats and wars aimed – and still aim – at imposing some sort of supremacy (cultural, religious, commercial, totalitarianism, etc.). They used to lead to servitude or slavery i.e.

the negation of alterity and siblings’ identity. In ancient times – and this is still the case in criminal activities such as pictured in so-called snuff movies – slaves and vulnerable people combated either other slaves or feral animals in circuses, until blood is poured and visible; this was championed by Antique Romans. Antique Greeks, whose civilization mentored Romans, feared blood inside cities: vivid – reddish – blood was to be poured by heroes in combats outside cities, and death penalties inside the cities were administered by poison as for Socrates [8]. This echoed an ancient fear very common in the Eastern Mediterranean civilizations, i.e. suffocation and bluish – poisoned – blood accumulation [9,10]; this stood for both citizens and domestic animals for food, a very wise precept to avoid pests; one barely remembers that religious rites of bleeding animals before sacrifice originate from this precept. Shakespeare portrayed in “the Merchant of Venice” the payment of a debt by “a pound of flesh”; indeed, most offenses requested that spilled blood erases such a debt: duels – that are still in force within Aristocracy in certain countries – define a conqueror and a looser, in general the one whose blood was poured (“fight to first blood”). Guerilla, terrorism also value much blood, whereas civilized states develop so-called “clean weapons”, meaning bloodless ones. Is art the acme of a civilization? If yes, do nowadays happenings – featuring the use of blood from self-inflicted wounds or collected from menses – stand for art or deviation of art? [11]. This remains an open question.

4. Blood and cults – from magic to anthropology

Anthropologically, blood appears as a living medium in magic and/or religious rituals, more powerful than any other body fluids. Every fetish or cult – or ritualized – instrument (the “balafon”, for example, in Burkina Faso) has been sprayed with animal or even human blood. As a mimic of the scorched blood, then darkens towards the brown color, instruments are tainted with a trace of “passage” of “infiltration” of viscous blood using e.g. cock feathers as an aspersorium. Thus, people can see and understand that through the transferred blood, the inert object has become animated. The animated fetish or instrument becomes alive in its own right, carrying a clean energy to protect the community of the living or to fight against the forces of evil. A magic charge, possibly hidden in the very heart of the object, can increase the power. The fetish is thus genuinely alive with some autonomy: blood superimposes to hair, teeth, bones, clothing from a deceased person having had acknowledged lifetime magic or religious power; power addition can also be provided by sediments from the grave of such a dead. The gift thus passes in the instrument, perpetuating the animation. This is passage rite and a redistribution of energy forces.

Blood is seen as part of the circulating energy, specific to humans and animals, a part of the individual who travels, who breaks up, spreads, moves, and which has therapeutic and protective (apoptotic) properties [12–14]. No life without blood, no magic object without bloody ablution: this liquid, the “sap of man” to use Jean Bernard’s formula, is necessary and obligatory not only for the consecration of the magical instrument, but also to its survival. That is to say the continuity of its efficiency, as a kind of transfusion

to maintain its vitality. Without an offering, the Greek divinities dwindled; the maintenance of relationships with humans through offerings was essential. Those divinities and their cults largely vanished when the rising Christianity helped ending up the cessation of sacrifices. Fetishes and magic/ritual instruments in sub-Saharan Africa are in some way similar because of the needed communication between worshipers and divinities through offerings (blood being one amongst the most powerful); in that case, gods and spirits are made appearing with some visible, palpable, and accessible form compared to Antique Mediterranean divinities [15].

5. Blood, spirituality and religions

This chapter has been the subject of a previous review of our group [1]. Most cosmogonies associated the origin of life on earth with deities' body fluids, and particularly blood. In one of the major cradles of humankind, i.e. Middle East, cults emerged which worshiped the remitting capacity of blood, principally of enemies; ones' blood happened to be versed to confess serious offenses. The Bible, throughout its more than 70 chapters written over 16 centenaries, and other historical documents, are valuable sources of information about religious practices in the Middle East, where monotheism emerged after a long fermentation. This civilization led to the emergence of monotheist cults that were further developed by Hebrews as in the Hebraic and then the Jewish cult, which itself sourced Christianity. After Abraham, no blood might be versed from human siblings to please God, but surrogates. White and pure animals were then sacrificed, their species and size depending on the family welfare. Derived from those cults and inbred with desert civilization, Islam has magnified this tradition in their worship of the diverted sacrifice of Isaac by father Abraham, and the sacrifice instead of the ram. Those monotheist cults which often refer to themselves as the religions from the Book edify their relationship with God on a sort of contract (alliances): specific recognition of elected people from God's side and worship, adoration and obeisance from the people's side. The Holy Book or words are transcripts from God to humans through Prophets and/or witnesses, as revelations. Jewish and later Muslim offer to God a minor and once for all bloody sacrifice, which is the young male circumcision (after which the boy can be named for the Jews) [16]. Christians tend to consider that the blood of Christ on the Holy Cross is the only sufficient blood and have not developed circumcision on religious grounds. Among Christians, Catholics have magnified the sense of Christ's blood as they celebrate it in each Eucharist as the true blood, under the appearance – by transubstantiation – of wine; reformed protestants acknowledge only the memory of it and this is one among the major causes of the split. Nevertheless, though not at the time of the Eucharist, Evangelist cults magnify the Christ's blood on the Cross as the sin eraser (based on a verse of the Revelation or Apocalypse Book of the Bible) [17,18]. Of note, syncretic cults such as African-American (of which Voodoo), reemphasize the need of visible blood, from animal sacrifices and perhaps in some cases from humans, as do Evil's cults [19]. No such other body part than blood is central in religious cults, as of yesterday and today, conferring to blood a unique status in human spirituality.

6. Blood, foods and beverages

Not many civilizations eat rare and raw meat. Several explanations can be proposed, the main one being perhaps the risk of bacterial and toxin contamination that is alleviated by cooking; raw flesh is indeed barely eatable and meat has better to be matured to get tenderness, exposing it to contamination unless preserved iced, salted, smoked or dried. Several civilizations indeed banned meat-flesh and poultry or wildfowl unless the animal has been bled, to

avoid eating suffocated animals' flesh with communicable pests, and to favor hygiene and cooking (also avoiding worms). Hygienic habits from desert peoples went to be ritualized to become religious prescriptions now well known as the Casher and Halal food rites [20]. Early Christians, whose faith was inlaid in the Jewish, adopted the Fish as a recognition symbol and a bloodless food to commemorate the Christ's sacrifice on Fridays and during Lent. A significant change was operated after the Council of Trent which endorsed the split of the Protestant Reform and proposed a counter-reform, rehabilitating flesh and blood, exemplified by the Sacrificed Lamb, symbol of Christ, with spills of blood remitting humans' sins. In parallel, blood backed on tables; a characteristic example was the blood sauce termed "*à la Royale*", on richest tables. The poor actually never stopped eating blood under the form of black pudding and the like, since this was a convenient source of renewable proteins as the animal could be bled repeatedly and not killed [20]. Blood happened to be a medicine for the anemics and the chlorotic or consumptive (tuberculosis infected) and animal blood was fetched from the slaughterhouses as illustrated in many 19th and early 20th century novels [21]. After the de-Christianization era, wines could be named again after blood, paralleling ancient rites; for example, a vineyard in the Rhône Valley in France stands by the name of "*le Sang du Peuple*" ("the blood of the people"); this denotes an interesting anthropological feature.

7. Bloodletting and blood transfusion

Bloodletting and blood transfusion have identical roots but divergent history. For years bloodletting was a panacea to treat different diseases, but was also applied to non-medical but spiritual reasons (as proposed by Saint-Bernard of Clairvaux [1090–1153] and Saint-Hildegard von Bingen [1098–1179]) [22]. The ritual, spiritual bloodletting is still existing [23]. Nowadays, medical bloodletting is performed under strict conditions in patients suffering polycythaemia rubra vera and hemochromatosis.

Perhaps intermediary between ritual letting and transfusion is the brotherhood ritual of exchanging blood, in which two or more people, typically males, intermingle their blood (from cuts) to breed families or clans.

The concept of blood transfusion is attested in very ancient civilizations [22]. The origin of the word transfusion stems from Latin (*transfundo*), which initially meant to pour from one vessel to another; its acception was early extended to two different meanings: the corruption of a population by foreign blood, with sexual and hybridization connotations, and the transfer of a debt (*Digesta justiniani*, 533 AD). Both sexuality taboos and the debt were thus initially present in the word transfusion [3,24]. In the Victorian period, the relationship between blood and sexuality was exemplified in the myth of Dracula: by draining blood from an innocent victim, the vampire transfers its damnation to the innocent "donor". The story of medical blood transfusion begins in 1628 with the description of the human blood flow system by William Harvey. Transfusion owes to the discoveries made in England in the 17th Century and then to the French. Jean-Baptiste Denis was the first to communicate his experience with animal to human blood transfusion, claiming in 1667 to have successfully used a transfusion of sheep blood to cure a 16-year-old boy suffering from fever. However, further attempts were unsuccessful, and one transfusion led to Denis being charged with murder although this death was ultimately found to have been caused by the victim's spouse and not influenced by the transfusion itself. The controversy led to the 1675 edict of the Châtelet prohibiting blood transfusion in humans. In 1829, James Blundell established the conditions for successful human-to-human blood transfusions. The modern history of blood transfusion really began in the early 1900s when Karl Landsteiner, investigated the major

blood groups [6]. Progresses were made all along the 20th century after WWI and next, during all military conflicts, reemphasizing the (eternal) issue of life and death through blood [25]. Transfusion still makes progresses, but years 2010 and over set up the non-transfusion preference exemplified by the concept of Patient Blood Management [26], at a time where transfusion has never been so safe [27].

8. Blood as a resource: whose ownership?

The issue of the ownership of one individual's blood is essential, as it commands collective behavior relative to wars; indeed, militaries' and often civilians' blood – either versed in combats or collected to rescue injured soldiers through transfusion – may belong to the “State”, or the “Party”; it also governs individual behavior, as for example the free willing to donate blood (for transfusion purpose). There are indeed grossly two mainstreams: the one states that blood is a public resource and the other one restricts blood to one's privacy [28,29]. For long, peoples' blood belonged to deities and/or monarchs (who stood to have either a divine ascent or to be the chosen ones); such blood was collectively spilled to worship, or to combat enemies, or to conquer new territories either for the empires' economy or for disseminating religious beliefs. This standpoint has been used to make blood donation mandatory in dictatorships and former communist countries. Enslaved populations have neither identity, possession nor private blood: they are the master's (this happened to be the case in colonies, military and other dictatorships, productivity economies of earliest modern times). A number of young militaries – not necessarily kamikaze or terrorists, but also from regular armies' – yet stand this point, merging patriot and religious beliefs (e.g. the percentage of worshipping Catholics within the French Army officers from far exceeds the one among the rest of the population). On the contrary, as individuality emerged, individual control upon one's blood (and other tissues), sexuality, fertility, and death, are claimed for. Very interestingly, in its Code for Ethics, the International Society of Blood Transfusion (ISBT) states that blood is a public resource [30], as to favor the not for-profit as opposed to the for-profit sector for blood collection, to promote voluntary and unpaid blood donation, and to ban the blood business (the red market) [31]. It may appear paradoxical that individual voluntariness associates to public resourcing. It is not intended here that the case is further presented, as it is the object of fierce societal debates on both economical and philosophical grounds (they are indeed large commercial interests behind). Nevertheless, comparators for public resources are usually material such as water, air, nature gifts (wilderness, flowers and plants, insects, etc.) or immaterial such as cultural and patrimonial goods. “And the substances that make up the blood that runs through the veins of men is the same in all”: this metaphor is true as from a humanistic standpoint, and biologically false as blood can exquisitely distinguish between two individuals, either siblings and even twins. Blood antigen collection is unique to one carrier, but transfusion is made possible because of many unsuccessful immune defense mechanisms in the recipient [32]. A philosophical debate would perhaps invent a third medium: the gift of a unique humane material to be fused within a patrimonial good at no value. While understandable for philosophers – of which ethicists examining the case of voluntary, non-remunerated, blood donation (VNRD) [33] – this is conflicting with overall economy because, for example, donated blood has no material value but a serious cost, making it even becoming a financial burden for the society (the final payer). The immaterial substance of blood is no good: it stood and may still stand for the unseparated blood that was e.g. transfused from arm-to-arm in emergency situations in compassion for a close relative (with later drifts, when components were separated and anonymity installed); on the opposite, the material substance

of blood can be a good: it stands e.g. for the clotting factors that are processed for non-urgent needs and overviewed by the industry and pharmacies. For some, there are boundaries between the two entities, while for others blood is unique and non-separable. Anytime humankind invented boundaries, humans next favored calls for war; there is indeed actually a fight between tenants of either position and the battlefield is the ethics ground.

9. Blood and fears – blood and hopes

Blood has sourced a large body of fears with evocations of wounds and death, lethal hemorrhagic baby deliveries, crimes, wars, terrorism and combats, catastrophes, feral word animal savagery (or fantasy), curses and black magic, suffocation and heart attack (and stroke), etc. Transfusion was next aimed at saving people, but happened at a time to become a killer itself, transmitting HIV, the virus inducing AIDS, the unbearable disease having appeared in the 1980s and since [34]. An illustration of blood borne fears is the common sense of malaise (and faints) while seeing – or even speaking of – blood; blood often makes people at least uncomfortable, or at most frightened. Blood has fueled a large body of frightening fairy tales such as Blue Baird, ogres, vampires, malefic creatures and zombies. Despite all Catholics worship the genuine presence of Christ's true blood in each celebrated Eucharist – and sometimes drink it under the appearance of wine – a large body of them do not really endorse this essential mystery and – like reformed protestants – behave as if the blessed wine only commemorates the Christ's blood. A fraction of Catholics, upon the example of born again-Christians and especially Evangelists, truly acknowledge the power of the Christ's once for all blood, with hope in its redemptory capacity. They usually give a large credit to the Apocalypse – the last Novel Testament book – which states that blood and water poured from Jesus Christ's pierced body on the Holy Cross – wipes out or washes one's sins. This is hope, but for a very limited fraction of the population. More pragmatically, blood is now scrutinized to teach about individual's habits and risks, both inherited and acquired in nature; blood carries drugs (plasma bound) and nanodrugs (red cell bound); new and promising therapies are blood derived and borne, such as CAR-T-cells, to cite one of the major progresses of the recent years in hematology [35,36]. A common feature of blood alongside the spectrum from fear to hope is that there is a body of magic in it, as all aspects for the good and the bad are quite uneasy to apprehend and, thus, fueled imagination instead of comprehension.

10. Is voluntary non-remunerated blood donation a novel religion?

Blood is not trivial; it is multifaceted. In a secular (as opposed to religious) environment, blood should have been reduced to its materiality; this is apparently not the case. Ethics, the avatar for moral has captured blood collection and donation to edict some new rules: blood must be given as a charity, from the well-being to the sick, anonymously and with no benefit other than the sense of having made the good. WHO, ISBT, the European Directory for the Quality of Medicines (from the Council of Europe) and other large professional associations and NGOs – the Red Cross and Crescent, to begin with – have firmly stated that VNRD must be the standard. WHO has urged countries to fulfill this goal by horizon 2020, now postponed to 2024 e.g. in the Middle East (reviewed in [37]). ISBT has engaged a dispute with Plasma Protein Therapeutic Association, representing the for-profit sector; (PPTA) advocates for an open market plasma collection to best adjust to the increasing needs in plasma derivatives in the populations [38]. The International Hemophilia Foundation and other large patient associations claim for systems – paid or unpaid – that fulfill the patients' needs.

Some economists indicate that the demand in plasma derivatives cannot be met by a state owned or overviewed system, contrary to industries inlaid in business models. Blood donor associations and most blood establishments collecting VNRD have postures resembling unions or political parties, with tribunes speaking for the mass. A major argument is that the private sector has allowed unacceptable situations exploiting the poor and the most vulnerable in plasma collection plants located principally in the USA while owned by companies registered in well-thinking countries such as Australia, Switzerland, Ireland and Spain, to cite the most famous. This situation resembles a novel form of slavery and anthropophagy, the rich absorbing the blood resources from the poor [39]. WHO – and the like – have also constantly ignored messages sent out by countries unable to reach 100% VNRD for organizational and cultural reasons [40]: such countries often rely on family or relative replacement donation, banned by so-called – blood self-sufficient – Northern countries. An interesting example was given at a time in an African setting claiming that remuneration could stand for a contract, mandating that the donor is and stays healthy [41] (very much resembling the one contract initiated in the 30s in France by Arnault Tzank). Paid donations (an oxymora), replacement donation, VNRD have chapels and chaplains. This is not surprising for those who outline the very special status of blood and its uses in the society and in medicine. Will this stand on the grounds of belief or will either economics or politics overcome the sense of humanity and make rational decision? This is a still open question.

11. Concluding remarks

Cornerstones between – on the one hand – medicine and physiology, and – on the other hand – anthropology and philosophy are passages, exemplified by birth and death. Passages are ritually associated with fluids and gases (not only air/oxygen but also “Pneuma”, Spirit); among fluids, semen, fat and blood stand are essential, with often transitional forms between them and with “Pneuma” [42,43]. Blood is indeed a tissue which passes physiological elements (warmth, nutrients, acid-base balance, etc.), emotions, fears, hopes (redemption, remission of the sins). Blood passed from humans to deities and – at the time of Christianity – from God to humans. (Donated) blood has been the cause of one of the largest sanitary scandals of the 20th century, which – despite medical and political practices that led to this tainted blood affairs were unacceptable – killed much less people than nosocomial infection in hospitals to take just another example alike in the pathophysiology. The large community of medical doctors in many disciplines, including laboratory medicine, cares of blood and it is to those authors’ – and others’ – large surprise that it is poorly questioned by this community, often in disconnection with their patients’ atavistic fears and feelings at large.

Disclosure of interest

The authors declare that they have no competing interest.

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