Bleeding-edge technology in cardiology - or the mixed blessings of phlebotomy throughout the ages

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Bloodletting in medicine is as old as mankind. Its survival in modern times and against all odds closely resembles an evolutionary pathway that involves step by step progress, with pay-offs and experience gained at each step to refine and improve its use. In order to continue to function in a changing environment and time, diverse applicability is a prerequisite. It is argued that bloodletting is embedded in our common subconscious memory and therefore we should not be surprised that its practice will pop up from time to time to remind us of the very roots of human medical thinking. (Neth Heart J 2010;18:218-22.)

Keywords: Cardiology; History; Phlebotomy

As excess bleeding and the risk of upper gastrointestinal bleeding with antithrombotic regimens constitute a primary concern in modern day cardiology, how distinct is the connotation with bloodletting as a well-known and widespread therapy in the past when doctors, at first sight in season and out of season, confronted their poor patients with the advantages of tapping blood. Nevertheless in those days too, our predecessors relied on some sort of guideline, balanced and well thought out, as may follow from a textbook dating from the 1760s.¹ Phlebotomy as a therapy has nowadays been driven back to the outskirts of critical care medicine and no longer seems to be worth mentioning. The long history attached to this peculiar practice, which dated to 1000 years BC, however, makes time travelling worthwhile as its usage has survived in modern times like an evolutionary path in the growth of idea. To find such a path that involves step by step progress, with pay-offs at each

step, and with experience gained at each step to refine and improve the use of phlebotomy, may provide insight into the development of modern medicine. This paper is an attempt to define such a path.

Current status

Nowadays, phlebotomy is indicated in specific circumstances and conditions, such as hereditary haemochromatosis, polycythemia vera, essential thrombocythemia and porphyria cutanea tarda, to reduce the amount of red blood cells.

Until recently regular bleeding was also the treatment of choice in cyanotic congenital heart disease with symptomatic erythrocytosis, but because repeated phlebotomy causes iron deficiency with microcytic erythrocytes, which increases the whole blood viscosity and therefore can potentially accentuate rather than decrease the risk of a cerebrovascular accident, this policy became less advisable.² There is consensus now that phlebotomy should only be used for the acute resolution of hyperviscosity symptoms.³ In the management of acute pulmonary oedema phlebotomy may still be of some use in reducing pulmonary capillary wedge pressure, especially when rapid action is required. Finally, phlebotomy is mentioned in connection with lung injury and circulatory overload as a complication of blood transfusion resulting in pulmonary oedema. In the setting of orthopaedic surgery, 1% of elderly patients undergoing hip or knee surgery seem to experience circulatory overload and then phlebotomy and supplemental oxygen are the key therapies.⁴

The growth of an idea

The story of bloodletting is indissolubly connected with medical tradition; it originated from magic and religious ceremonies. The physician and priest were one and the same since disease was thought to be caused by supernatural causes. Witch doctors and sorcerers were called on to drive out the evil spirits and demons. Bloodletting was a method for cleansing the body of ill-defined impurities and ex-

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cess fluid. The early instruments included thorns, pointed sticks and bones, sharp pieces of flint or shell, and even sharply pointed shark's teeth. Miniature bow and arrow devices for bloodletting have been found in South America and New Guinea. A small bloodletting instrument resembling a cross-bow was once used in Greece and Malta. Wall paintings dating from 1400 BC depict the use of leeches for drawing blood from human beings.⁵

The beginning

The Egyptians practised bloodletting 1000 years BC and then this tradition spread to the Greeks and Romans, who embedded its usage in their concept of health and disease. At first bloodletting was supposed to literally facilitate the release of evil spirits from the body but later on the Hippocratic-Galen doctrine which lasted until the 16th century provided a physiological reason in a logical and clearly defined framework. At that time bloodletting evolved from ceremonial use and witchcraft to a logical and therapeutic act, based on knowledge, skill and idea, based on the theory of the four bodily fluids or humours, blood, yellow bile, black bile and mucus. According to this theory, the four elements in nature, air, fire, earth and water with their specific qualities determine one of four temperaments (sanguinic, choleric, melancholic and phlegmatic) which in turn depend on the equilibrium between the humours.⁶ The perfect temperament resulted when none of these humours dominated. A sanguine personality, for example, was presupposed to depend on the quality of the element of air (wet and hot). He or she is generally light hearted, social, spontaneous and confident, but can be arrogant, impulsive and indulgent too. Illness was understood as a dyscrasia or disruption of this delicate equilibrium and therapy was chosen on the basis of the prevailing humour. Sanguinistic symptoms (pain, fever, inflammation, dropsy as excess of water, but for instance exaltation too) point in the direction of excess of blood which made bloodletting logical and feasible at the time.

Blood is thicker than water

Ancient medicine based on Hellenic humanism held out little or no hope for desperate cases and therefore gradually became inflamed by the spirituality of Christian charity, eventually leading to a new kind or monastic medicine. In the middle ages, the philosophy of Aristotle gained new ground in the schools of Western Europe. In the 13th century this scholastic philosophy became the dominant influence in theology and above all in the work of Thomas Aquinas (1225-1274), whose teaching became the official doctrine of Roman Catholicism. Aquinas, however, was not only a commentator; he also developed his own views which are found in his theological writings. Above all, Aquinas ad-

Figure 1. Mediaeval bloodletting.

opted a new approach to the metaphysical problem of being.⁷ In the meanwhile, monastic medicine had taken a dim view on the practice of bloodletting. The attitude of the early Fathers toward the body is well expressed by Jerome. 'Does your skin roughen without baths? Who is once washed in the blood of Christ needs not wash again.' In this unfavourable medium for its growth, science was simply disregarded, not in any hostile spirit, but as unnecessary.⁸

Who for heaven's sake then would cure you of your ills? Blood is thicker than water and barber surgeons as all-round men stepped into this gap in the market and literally made the most of it.

Implementation of new ideas

For some of us it seems as if medical history started in the 19th century with the discovery of all sorts of pathogens. What happened before is for convenience's sake considered to be rather trivial and certainly nothing to be proud about. Nevertheless and for those who have an eye for it great progress was made with empirical power as a major driving force. Initially, scholars tried to reconcile new ideas and observations with ancient medicine but more and more a scientific approach became visible where intellectual development in itself got the upper hand and autopsy, anatomy and bedside teaching became standard features in medical education and progress with an ongoing challenge of the humour lore as result. New therapies and herbs became available after the discovery of the new

Figure 2. Bloodletting in the 17th century.

world and were eagerly put into practice like, for instance, *Ipocacuanha* powder, a purgative found in South America and described in *The Pilgrims* of Samuel Purchas.⁹

How folkloric or even grotesque the herbal therapy and prescriptions in those days may seem in our eyes, in order to survive, some kind of beneficial effect, also explainable with today's knowledge, could be anticipated.¹⁰ So bloodletting, at first sight applied in season and out of season, must have an objective beneficial effect in sickness (besides the emergency situations mentioned in the introduction) by current standards too, and there is!

Validation by tradition and experience

Blood donors show higher levels of wellbeing compared with controls as indicated by better mood, higher vigilance and relaxation.¹¹ Of course donors are healthy and therefore the observation that the decrease in systolic blood pressure and flow and the increase in vascular resistance after phlebotomy were similar in real bloodletting and in phlebotomy simulated by means of verbal hypnotic suggestions is of more interest, suggesting a psychic influence.

Mere hypnosis without the suggestion of phlebotomy and simple bed rest did not produce any effect. These results indicate that the haemodynamic changes observed during and after a blood loss are partly due to mental involvement rather than merely to the hydraulic effects of the removal of blood.¹² More evidence for cerebral reactivity comes from the fact that haemodilution after phlebotomy does not improve oxygen transport or tissue oxygenation in the normal human brain, although there is a marked increase in cerebral blood flow,¹³ improving alertness which correlated very well with the observed augmentation in flow.¹⁴ In essential hypertension resistant to a standard triple combination of antihypertensive drugs, phlebotomy significantly lowered mean arterial pressure after 14 days, while the duration of this hypotensive effect lasted about four weeks.¹⁵ Finally, bloodletting therapy has been used for its pain-relieving and heat-reducing effects when treating adjuvant arthritis. It may reduce heat and pain through its regulating action on the content of proteins such as interleukin in the local diseased area as measured by radioimmunoassay.¹⁶ Moreover, it has been demonstrated that haemodilution is an efficient conservative therapy in peripheral arterial occlusive disease, where a single isovolaemic haemodilution (replacement of 500 ml blood for an isotonic sodium chloride solution) increased the pain-free walking distance by 85%.¹⁷

Step by step explanation and application of new techniques such as microscopy provided a better understanding of the (patho)physiology involved, along with a growth of idea in general. The use of bloodletting in hypertension, apoplexy, dropsy and nervous disorders, as promoted in Tissot's manual, can then be considered a hinge to modern medicine.

State of the art, guided by Tissot

Dr Samuel Auguste David Tissot (1728-1797) will not be found in any medical history canon, despite the fact that he was renowned for his ideas on migraine. In his lifetime, however, he was a phenomenon against his will after the publication of '*Avis au peuple sur sa sante*' in 1761. It certainly supplied a long-felt need as became apparent from an English translation from 1765: '*I had intended it only for a small Extent of Country with a moderate Number of Inhabitants; and was greatly surprised to find that within five or six Months after its Publication it was become one of the most extensively published Books in Europe; and one of those Treatises, on a scientific Subject which has been perused by the greatest Number of Readers of all Ranks and Conditions*'. Tissot advocated bloodletting in four cases: excess of blood in the body, inflammatory disease, impending inflammation after wounds and bruises and excessive pain ('in order to appease and moderate the pain, and

thereby to obtain time for destroying the cause of it by other remedies'). He then elaborated on the cause of excess of blood:

'If he takes but little exercise, sleeps much and has not been subject to any very considerable evacuation; the total stopping or long interruption of some involuntary bleeding or haemorrhage to which he had been accustomed; a full and strong pulse, and veins visible filled with blood in a body, not lean and thin and when he is not heated; a florid lively ruddiness; a considerable and unusual numbness, sleep more profound, of more duration and yet less tranquil and calm than at other times; palpitations sometimes accompanied with a slight fainting fit, especially on being in any hot place; vertigos or swimings of the head, especially on bowing down and raising it up at once; frequent pains in the head to which the person was not formerly subject; an evident sensation of heat, diffused over the whole body; a smarting sort of itching all over and lastly frequent haemorrhages and these attended with manifest relief and more vivacity'.

He then points out that many of these symptoms must concur in order to perform a first or even second bleeding with effect. Those who have an eye for it will recognise the clinical signs of a sedentary lifestyle, pruritus (as a major clinical problem in patients with polycythaemia vera), hypertension and unsteadiness, dizziness and vertigo which happen to occur more frequently in hypertensive subjects,¹⁸ all of which in one way or another may take some benefit from bloodletting according to current insight.

Finally we must not forget that to this very day cupping bloodletting is still a widely used remedy in traditional Chinese medicine in preventing diseases and the treatment of the diseases induced by excessive heat and blood stasis.¹⁹

Figure 3. Educationally efficient self-directed learning of phlebotomy procedures.

The hiccup in conclusion

In evolution tiny changes in a small part of the vast cellular DNA pool and natural selection ensure development without design or greater purpose. The growth of idea may be approached in the same way, as the result of a natural development in learning by doing. The act of bloodletting seems a trait that is deeply anchored in our common subconscious memory; it is locked up in our genes. In all objectivity its effect is more psychological than physical but nevertheless it survived against all odds and like, for instance, the development of the eye, this idea of cleansing the body from 'evil' was reinvented several times as a 'general purpose' therapeutic at least in Western medicine. For in the 19th century Louis, a so-called pre-formal epidemiologist, concluded that there were useful effects of bloodletting, but only for a few specific indications: *'Thus, the study of the general and local symptoms, the mortality and variations in the mean duration of pneumonitis, according to the period at which bloodletting was instituted, all establish narrow limits to the utility of this mode of treatment'*.²⁰ Evidence-based medicine avant la lettre already denounced widespread practice at that time. But the fire never extinguished as will be apparent from a whole new line of investigation to find out if blood loss does in fact lower the risk of heart disease by reducing the storage of iron, which is believed to act as a catalyst in cholesterol oxidation.²¹

Moreover, we have become accustomed to the phenomenon of blood doping as reinfusion of autologous blood after phlebotomy significantly increased exercise tolerance.²² Later on, erythropoietin and genetic engineering entered the medical arena. Undiscriminated increment of haemoglobin levels, however, seems to correlate with an increased risk for adverse outcomes in different patient groups.²³ Therefore, phlebotomy (in order to maintain haemoglobin) played a key role in the EPOCARES study, a Dutch Heart Foundation-funded trial that examines the role of erythropoietin in combined heart and renal failure, making the full circle once more.

It seems that we are stuck with the idea of bloodletting as a beneficial tool, as a evolutionary remnant in medical thinking like the hiccup, a small heritage from the early amphibians using precisely this mechanism to shut down their lungs when they switched on gill respiration.²⁴ An archaic system that is still stored in our brainstem today, with all the consequences to it. So, willing or not, the practice of bloodletting too will pop up from time to time to remind us of the very roots of human medical thinking. ■

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