THE FORTUNES OF HAEMOPHILIACS IN THE NINETEENTH CENTURY

by

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WHEN the final history of haemophilia is written it will be divided into three parts. The first part will describe the era of clinical observation and ineffectual treatment. The second part will deal with an age of increasingly effective medical management and better understanding of the underlying mechanisms of haemophilia. The third and final chapter has yet to come. Not until the disease can be permanently suppressed or, at least, controlled in the manner in which insulin restores the disturbed physiology of a diabetic will the haemophiliac face life on equal terms with his healthy colleagues.

The early chapters will be considered here, mainly from the patient's point of view. The period covered is from 1793 until about 1910. Prior to 1793 there were several case reports highly suggestive of haemophilia, notably in the *Talmud* and a text ascribed to Alsaharavius. It is surprising that such a spectacular disease was not recorded by the gifted observers of the Renaissance and afterwards, particularly as retrospective inquiry into the pedigrees of several large haemophilic families has disclosed evidence of affected members extending well back into the seventeenth century. However, in 1793 the first clear description of a bleeding disease affecting males and sparing females was published by an anonymous author, almost certainly G. W. Consbruch of Bielefeld in Westphalia.[1] The report appeared in an obscure German text[2] and for this reason credit is usually given to the Philadelphian, J. C. Otto,[3] whose similar account entered the newly founded circulating medical literature ten years later and so received widespread attention.

A century later the first positive measure to combat the persistent and not easily controllable haemorrhage of haemophilia became available. Largely due to Landsteiner, blood transfusion had become a safe procedure. Unfortunately, it was by no means the therapeutic answer, but at least provided a rational approach to treatment.

How patients fared in the days before blood transfusion is not without contemporary significance. There are many haemophiliacs living today whose lives have been influenced by the attitudes of relatives on the maternal side of their family. Memories and, in some cases, personal experiences extend back to the time when medicine could offer little to control bleeding. In these families a legacy of anxiety, despair and lack of faith in the medical profession has been handed down with the haemorrhagic trait, often with equally crippling results.

An outstanding feature of haemophilia commented on by all the early writers is the trivial nature of injury that often precedes bleeding. In the tenth century, Alsaharavius[4] remarked on this when he visited a Spanish village where the youths bled to death after insignificant wounds. The barber mentioned by Alexander Benedictus[5] in 1539 is traditionally considered a haemophiliac. He died miserably from haemorrhage after scratching his nose with

scissors. Most authors held that some degree of trauma was necessary to precipitate bleeding, although instances occurred where no obvious injury had taken place. These apparently spontaneous haemorrhages (called Spontanblutung by Schloessmann[6]) were later recognized as characteristic of severe haemophilia. In 1844 Erdmann[7] astutely observed that there were recurring periods of increased susceptibility to bleeding, the *orgasmus sanguinis*. Over a century later an anonymous haemophiliac writing in the *Lancet* complained that no physician would believe he suffered from cyclical 'bleeding phases'.[8] These observations underline the perilous situation that arises when an individual lacks a competent defence against the loss of blood.

The physical hazards confronting a haemophiliac have not changed over the years, although the actual source of injury has varied. The motor-car has replaced the horse-drawn wagon[9] and hay cart[10] as an instrument of destruction. The haemophilic infant of 1860 cut his mouth on a wooden cigar holder and bled to death.[11] In 1961 the infant ingests 'the detached metal tip of a bathinette drainage hose' and was saved by modern surgery and temporary complete restoration of the clotting defect.[12] Animals formerly caused much injury. Falls from a horse were common and kicks resulted in lacerations which on one occasion led to the death of thirty-three-year-old Dr. Swain, a member of the Massachusetts family first described by Hay[13] and later made famous by Osler.[14] Vieli[15] reported the fate of two haemophilic boys kicked by a cow. One died from exsanguination and the other survived an enormous perineal haematoma. The falls and knocks of everyday life were the most common cause of serious bleeding. Lossen[11] described incidents leading to the death of fifteen haemophiliacs who lived between 1796 and 1904 (Table 1). They were all members of the Mampel family, poor rural labourers living at Kirchheim near Heidelberg. Direct injury from falls or hard objects caused fatal haemorrhage in over half the cases. Bleeding from mucous membranes, surgical interference and intercurrent infection accounted for the remainder.

TABLE ONE

AGE AND CAUSE OF DEATH IN 15 HAEMOPHILIACS OF THE MAMPEL FAMILY 1796–1904[11]

Age	*Cause of death*
Infancy	Epistaxis
9 months	Fell against coal scuttle.
1 year	Oral haemorrhage after hitting mouth against a door.
1	Cauterization of gums.
2	Haemorrhage.
3	Lacerated lip after fall.
3	Run over by a wagon.
7	After a fall.
7	Oral haemorrhage after a fall with wood in mouth.
8	Fell off chair.
8	Tooth extraction.
14	Fell while jumping over a tree trunk.
23	Haematuria, after drinking new wine.
25	Pneumonia.
35	Bleeding after falling over a heap of stones while drunk.

Another source of danger lay in local customs and cultural practices. Vieli[15] mentioned a small Swiss boy 'who bled and was constantly bruised by the blows received in the games by which Swiss children harden themselves and foster their courage'. The ritual of circumcision often proved fatal. In an Ukranian Jewish family ten boys from two generations bled to death after the operation.[16] Grandidier[17] described a family where two out of five brothers died from circumcision, and remarks that at least one boy in the next generation was not circumcised, although he remained of the Jewish faith. In another of his families the parents became Christians after the death of their first two sons, and subsequent boys were spared circumcision. There are some relevant passages in the *Talmud* on circumcision when there is abnormal bleeding in the family. Rothschild,[18] who carefully studied the text in an early version of the *Talmud*, concluded that haemophilia was the only disease that could be involved. In the *Tractate Yebamoth* (folio 64) the story is told of four sisters of Zipporah who lived in the second century A.D. The eldest sister had her son circumcised and he died. The same fate befell the first-born sons of the second and third sisters. When the fourth sister took her son to the Rabbi Simon ben Gamaliel he ordered that she should not have him circumcised lest he also die. In the *Tractate Shabboth* (folio 134a) the Rabbi Nathan dealt with a similar situation.

It was not surprising that haemophilia came to be regarded as mainly a disease of male children. In 1826 Davis[19] wrote of a labouring family from Bristol that none of the affected males had reached man's estate. A few years later, with reference to the haemophilic son of the foremost family in the land (Prince Leopold, Duke of Albany), '. . . it was whispered at court that he, whom all found perfectly charming, would not attain the age of manhood, or that if he did he would not be normal'.[20] In 1855 Grandidier calculated that half of all haemophiliacs died before their seventh year. Just before blood transfusion became available Carrière[21] estimated from his own group of patients that only 11 per cent reached their twentieth year.

Besides not appreciating environmental dangers, children had other attributes that weighed against a life free from haemorrhage. Youthful exuberance led one of Fischer's[22] young patients to spring into a vat and develop prolonged, almost fatal, bleeding. Haemorrhage followed forbidden pastimes, including epistaxis after firing rockets,[23] extensive haematoma of the calf on playing football[24] and serious bruising of the arm while swinging on a rope.[25] A tragic death occurred when a nine-year-old haemophiliac threw a piece of slate at his infant brother who succumbed to the resulting haemorrhage.[26] Several authors wrote despairingly of the perennial problem of haemophilic children being involved in rough play and fights with their companions. This was aggravated by the majority having a normal appearance. Restrictive measures were not usually successful as Delmas[27] found when his young patient became covered with ecchymoses if he played with a ball, but on confining the child to sitting in his room, bruises developed over the buttocks and thighs.

There was no sure way of avoiding haemorrhage, although one man who spent his life in an arm-chair managed to outlive his affected relatives by thirty years.[27] Some parents trained their children to show a Pavlovian response to

dangerous objects. The boys of the Litchfield family in Connecticut were said to show 'an extreme sensibility in relation to their dangers, shuddering at the sight of edge tools and avoiding with the utmost caution all exposure to them'.[28] Pickells[29] reported a family where two brothers had died from bleeding, one after a lacerated thumb and the other from a sickle injury. The third brother became so terrified of sharp instruments that he made his wife cut up his food at meal-time.

Parents and other close relatives frequently lived in a state of constant fear and anxiety. There was always the chance that they would be confronted with a situation similar to that recorded by Stahel.[30] A small haemophilic boy suffered an insignificant abrasion. His parents were unable to control the persistent bleeding and could not obtain medical attention. Powerless to help, they could only watch with horror until 'at the end he died quite quietly'. Wright[31] gave a graphic description from his practice in London. 'The perfectly desperate condition that things get into in the houses of the poor when such bleeding as this occurs is more easily imagined than described. I have seen a room look like a shambles and know a case where a mother finding her boy bleeding in his sleep had to wrap him in the blood-soaked blanket and to wheel him on a coster's hand cart all the way from a suburb to one of the London hospitals.' However, getting to a hospital did not necessarily benefit the patient. Hey Groves[32] mentions one who, bleeding from the mouth, 'walked about from doctor to doctor trying each new remedy until at last he found refuge in the infirmary only to die from the resulting anaemia'.

Feelings of guilt plagued mothers of haemophiliacs. External agencies were invoked to account for the birth of an affected son as, for example, attempted rape[9] or being frightened by a thunderstorm[33] during pregnancy.

The last Empress of Russia was aware that her marriage to Tsar Nicholas II was opposed by his father on the grounds that she was a sister of the haemophiliac, Frederick William of Hesse, and therefore likely to transmit the disease to the Romanoff heir. When the Tsarevich was born with haemophilia the Empress desperately sought a cure from leading European physicians until at last she turned to Rasputin. Her mother, Princess Alice of Hesse, never forgave herself for not providing protection to an upper story window through which Prince Frederick William fell to his death. The Prince's elder brother also considered himself partly responsible for the tragedy and was overcome with grief and troubled by nightmares for many months afterwards.[34]

In the nineteenth century the attitude of the medical profession towards haemophilia was that of Ambroise Paré's ancient Doctor, who wrote 'That as in Nature so in disease there are also Monsters'.[35]

The physiological basis of the disease was not well understood. John Hunter had called blood-clotting 'an operation of life', and careful observers noticed that blood shed by haemophiliacs did not coagulate in a normal manner.[36] In 1863 Joseph Lister[37] wrote that the study of blood-clotting engaged the best energies of many very able men and the outline of modern blood coagulation theory was evolved towards the end of the nineteenth century.[38] Nevertheless pathologists continued to produce evidence suggesting that an abnormality of

blood-vessels was responsible for disordered haemostasis in haemophilia.[39] Practising physicians developed their own theories. Watson[40] held that the inherited haemorrhagic diathesis of males was due to a type of vicarious menstruation similar to that seen in certain women. This view was based on phrenological observations made by M. Gall. In 1891 when Wright[41] showed that the time taken for haemophilic blood to clot in glass tubes was constantly prolonged, attention became permanently focused on the blood-clotting system.

Nineteenth-century methods for dealing with haemophilic bleeding were usually ineffectual. On the only recorded occasion that human blood transfusion was used, it was dramatically successful. In 1840 Lane[42] performed Dieffenbach's operation for squint on an eleven-year-old boy without prior knowledge of a classical history of abnormal bleeding. Haemorrhage commenced shortly after the operation and continued almost unabated for six days when 'the skin was of the paleness and almost coldness of death and the pulse could not be felt at the wrist'. Direct transfusion of twelve ounces of blood from a stout young woman was commenced. Bleeding ceased and shortly afterwards the boy sat up, drank a glass of wine and eventually regained perfect health. This first fortuitous success of blood transfusion in haemophilia would not have occurred had not Lane shown great skill and patience in using the primitive apparatus.

There were three approaches to arresting haemorrhage. Either conventional methods, empirical remedies or no specific treatment at all were used. Some experienced physicians preferred the latter approach. Wickham Legg[43] wrote that '. . . one of the most satisfactory ways of treating bleedings is to leave them to themselves, and when the patient is blanched and exsanguine, they cease'. There are many reports of adolescent or young adult haemophiliacs surviving a period of extreme exsanguination. However, small children were unable to withstand repeated blood loss so well. This is illustrated by Rieken's[44] case, a child aged three. He developed a haemarthrosis of the left knee which caused him to fall and cut his tongue. 'Blood gushed from his mouth and the cautery was applied thrice without effect, the bleeding continuing for seven days until he was like a wax doll in appearance. Within a fortnight after it ultimately stopped he had a copious epistaxis and died with convulsions on the third day.'

Blood-letting in its various forms claimed many victims. Haemorrhage from the bites of leeches applied to a haemarthrosis proved fatal.[45] One young patient had a single leech attached to a periorbital haematoma. This led to prolonged bleeding, infection and eventual destruction of the eye.[46] Cupping was performed on a nine-year-old haemophiliac for some affection of the knee-joint (presumably haemarthrosis). On returning home bleeding recommenced, but was allowed to continue as being beneficial. The boy died the next day from the effects of blood loss.[47] Several haemophiliacs died from bleeding at the site of a venesection wound.[13, 48] Therapeutic blood-letting was frequently combined with other dangerous remedies, and it is not always clear what caused the patient's death. Vieli[15] attended the fifty-five-year-old Gartmann of Tenna who had been bleeding for a month from a tooth socket. Application of lapis infernalis, sulphuric acid and creosote were of no avail. Compression of the

carotid artery and cupping caused syncope and convulsions. Several days later the patient died.

Some procedures not ordinarily followed by haemorrhage led to fatal bleeding when performed on haemophiliacs. In this manner two patients died after the application of blisters.[49] Several physicians published clear warnings of the danger and futility of blood-letting in haemophilia.[50] Yet the practice was widespread. In 1876 Heath[51] reported part of a conference on haemophilia in which Sir W. Jenner asked A. P. Stewart if he had carried out bleeding every few weeks to relieve plethora. Stewart replied that he had on five or six haemophiliacs, but all of them were now dead. In 1894 when blood transfusion was still unsafe, Osler[52] could recommend nothing more for the treatment of haemophilia than that some authorities advised venesection.

Some patients were aware of therapeutic hazards. One thirty-four-year-old haemophiliac with the aid of his friends successfully opposed venesection for a violent fever on the grounds that he was a bleeder.[53] Ulrich[54] mentioned a patient who was reluctant to have leeches applied to a haemarthrosis of the elbow because of a previous experience. He was overruled and nearly lost his life from the ensuing haemorrhage. Another unwilling patient was unfortunate to enter the last citadel of massive blood-letting. Riccord of the Salpêtrière attached twenty-five leeches to his perineum with disastrous results.[55]

Surgery was an ever-present danger. Only a few surgeons like Liston and Hey Groves seemed fully aware that unless an operation was performed in a bloodless manner the haemophiliac was certain to die. Thus Liston[36] most carefully opened an abscess in the groin of a severe bleeder using blunt dissection and the chemical cautery. Fatal haemorrhage followed operations for trivial reasons such as circumcision[17] and the relief of tongue-tie.[56] Ligation of an artery was common practice to arrest bleeding and haemorrhage from the incised vessel caused death.[57] One of the most hazardous situations for the patient was to seek surgical relief for haemarthrosis. It was conventional for a painful swollen joint to be incised and the inevitable bleeding was more often fatal than not. In 1890 König[58] showed a striking loyalty to the surgery of his day for after giving what has become the classical description of haemophilic arthritis he opened the knee-joints of two patients, and both subsequently died from blood loss. As blood-letting was forced on patients so were operations. Durham[59] recorded the death of a boy after lithotomy despite the family pleading with the surgeon to avoid operating because of an abnormal bleeding tendency in the child and his male relatives. Another patient went to his general practitioner for relief of an aching tooth. The physician, aware of the boy's past history, refused extraction and advised dental consultation for non-operative treatment. The dentist, in full knowledge of the consequences, removed the tooth and the boy died a few days later.[60]

The barren therapeutic outlook led physicians to become enthusiastic over any form of treatment that seemed at all promising. A substance, often with no apparent relation to haemostasis, was administered to a haemophiliac. If its use coincided with cessation of bleeding it was energetically promoted for a while until its uselessness became obvious and then, unless perpetuated by commercial

exploitation, it was soon forgotten. Hey Groves[32] made his attitude to such empirical theory quite clear. Referring to haematuria in a haemophiliac, he wrote '. . . it stopped spontaneously, or perhaps I ought to say as a result of taking drugs'. The experience of Cochrane[61] in 1841 is typical in illustrating the genesis of a new remedy. After initial failure to control bleeding from a boy's tooth socket with a bottle of port wine daily, used in conjunction with kino and succus japonicus, he attributed eventual recovery to wrapping the patient in Peruvian bark quilted between two folds of cambric. Subsequently faced with a similar case when this and other forms of treatment failed, Cochrane tried tincture of iron muriate which was instantly successful. He concluded that this latter agent would exclude all anxiety when dealing with the next patient.

There were a few successes with heroic forms of treatment. Lane's blood transfusion has already been mentioned. Fischer[22] recorded the rather incredible arrest of gastro-intestinal haemorrhage after transfusion with 150 grammes of lamb's blood. A sister of a small boy eventually controlled bleeding from a tooth socket by maintaining continuous digital compression for 72 hours.[62] In 1913 a Swedish physician exerted manual pressure on the site of an above-elbow amputation 'night and day'. Haemorrhage ceased and the patient lived to be examined by Sköld in 1944.[63] However, it is probable that the experience of the family reported by Davis[19] was typical of this era: '. . . various means had been tried to remedy this evil until at last the parents abandoned all hope of averting the progress of the malady and had been accustomed for some time past to leave the care to Nature'.

Some families who could obtain no effective treatment from the medical profession turned to practitioners of other arts. Krimer's[64] patient was given up for dead after tooth extraction. The relatives consulted a man who practised 'a sort of magnetism'. He made passes over the dying man's face and then called on God, whereupon the bleeding stopped. Some time later the magician successfully arrested another haemorrhage by the same means. The most famous of all non-medical men was Rasputin. The ignorant peasant exerted a soothing or hypnotic influence over the Tsarevich's painful symptoms and was accredited with their control.[65] He was said to be effective even over the telephone.[34]

The poor prognosis and ineffectual medical treatment meant that the few haemophiliacs who reached adulthood could hardly compete on level terms with their contemporaries. For one patient, this was made quite clear. A leading article in the *British Medical Journal* of 1868[66] recommended that Prince Leopold, who at the time was convalescing after a haemorrhage, should abstain from violent exertion. The *Journal* suggested that he become a patron of the arts and literature. The Prince did his best to support the arts, although handicapped by recurrent haemarthroses in one knee-joint.[67] Ironically, it was while attending a floral and musical festival at Cannes that he fell and struck his head. Later that night an aide-de-camp was awakened by stertorous breathing and found the Prince having convulsions. He was paralysed on one side and died, presumably from an intracranial haemorrhage.[68]

It was difficult for the average patient to become a self-supporting member of society. No facilities were available to direct the haemophiliac into an

occupation free from obvious sources of trauma, and hazards existed in almost every type of employment. Of two haemophilic physicians, one could hardly follow his profession[69] and the other had great difficulty in completing a term of hospital residency.[70] Clerical workers developed bruises due to prolonged sitting or resting an elbow on the desk.[27] In trades where sharp instruments were used, occupational trauma led to serious bleeding. A weaver[71] and barber[72] suffered in this manner. Hey Groves[32] described the fate of a shoemaker who 'as is the habit of these workers, kept the nails which he was about to drive into the shoe, in his mouth. The point of one of these penetrated his gums and after twenty days bleeding he died of anaemia'. Barlow[73] thought it strange that his patient, a lamplighter, had not developed haemorrhage into the shoulder-joints from raising a pole to the gas lights. This happened to a haemophilic sculptor,[63] so a more strenuous use of the arms is probably required. Another of Hey Groves's patients[32] illustrated the difficulty a haemophiliac had in remaining employed. The man was a tram conductor who developed Volkmann's ischaemic contracture after haemorrhage into the right forearm. Function partially returned but inability to supinate the forearm rendered collection of fares difficult because the palm could not be turned uppermost. The patient was forced to resign his position with the trams. On applying for railway service both his haemophilia and deformity would have been overlooked had he not been asked to cover the right eye. This he did with the knuckles and so was detected.

There is little written on how haemophiliacs fitted into the social life of the nineteenth century. Many who survived childhood were physically disabled, and so were presumably regarded as cripples. Stahel[30] sketched the appearance of two patients. The elder one, aged fifty-eight '. . . was very bent, with a large knob like cyanotic nose. Teeth defective and carious; gums swollen, dark red and softened; creaking in joints and limitation of movements.' The other, a younger adult, had '. . . lips slightly blue, bad teeth, swollen gums receding from teeth. Muscles of both arms very atrophic; defective movements of legs and arms, very lame.' In contrast many haemophilic children were described as having a healthy appearance, often in a manner which suggested that the writer considered this incompatible with such a distressing disease. From evidence in their monumental survey, Bulloch and Fildes[1] concluded that young haemophiliacs usually had a gay and reckless nature. But this was not always so. Wachsmuth[74] had a young patient whose outbursts of rage seriously interfered with treatment. Some interesting features of the haemophilic personality were recorded in the exchange between Ross and Dent, which took place in the correspondence columns of the *British Medical Journal* in 1898.[75, 76, 77] Ross described a twenty-eight-year-old haemophiliac who nearly died from haemorrhage following drainage of an abscess. It was only as he was recovering that the patient told his agitated physician he was a bleeder. Ross felt this experience warranted that all haemophiliacs should be tattooed with the name of their disease. In reply, Dent wrote that tattooing was dangerous and the patient was unlikely to give his consent. He then enlarged on 'the constant mental peculiarities of definite form in bleeders', of which the most common was '. . . an inability,

more than an unwillingness to tell the truth about their condition even after alarming experiences with it'. He described a sixteen-year-old boy who continued to bleed from a tooth socket despite all treatment. The medical attendants were certain he had haemophilia, but the boy stoutly denied any abnormal bleeding tendency. Eventually his mother was called, who told of her son's numerous haemorrhages. However, 'the youth furiously resented his mother's appearance at the bedside and actually died cursing her and all around him, and asserting with his last breath that he did not bleed more than others'. Dent concluded that haemophiliacs were a menace and should wear their diagnosis as a label around the neck. Ross replied that a label was no good as the patient would soon remove it. He mentioned some other haemophiliacs. Two were liars, and the third so bad tempered that his parents would rather he died than have to live with him at home.

Those that were not disabled and tried to compete on level terms with their contemporaries usually paid the penalty. A twenty-two-year-old medical student from Stuttgart engaged in a duel despite full knowledge of his bleeding diathesis. He died two days later from uncontrollable haemorrhage caused by a sabre wound.[78] Wright[31] wrote the epitaph of a nineteen-year-old haemophiliac. 'Died of haemorrhage after amputation of leg necessitated by mortification brought on by blow of cricket ball.' One member of Nettleship's[79] family died from gastro-intestinal haemorrhage following competitive rowing. A fish-hook wound and an injury received while playing hockey nearly accounted for two other brothers. Several members of a large haemophilic kindred from Württemberg were conscripted into the army during the Napoleonic and Franco-Prussian wars.[22] One man survived several wounds received in battle, only to die of bleeding from a tooth socket at the age of sixty-two. Two others were discharged because of abnormal haemorrhage, one after tooth extraction, the other on developing haemarthrosis.

The haemophiliac who considered marriage was hampered not only by the prospect of an early death and economic insecurity but also by opposition from the medical profession.[14] So few married that Bulloch and Fildes[1] with all the pedigrees of the nineteenth century at their disposal were unable to comment on the transmission of haemophilia to the sons of haemophiliacs. Muir described a large South African family whose ancestors reached the Cape in 1660.[80] He accounted for twelve generations containing 610 normal individuals and 46 haemophiliacs. Only 4 of the latter married as compared with practically all their normal male relatives. There is, however, a record of a severe haemophiliac being married twice[17] and one of Fischer's[22] patients, despite numerous almost fatal haemorrhages, married his deceased normal brother's wife.

The belief that haemophilia was perpetuated by symptomless female carriers of the gene provoked much opposition to any woman from a haemophilic family marrying. Physicians,[52] parents[81] and even the unfortunate women themselves[82] advised strongly against such a union.

For the haemophiliac, the nineteenth century ended as it had begun. There was a wealth of information on the natural history of haemophilia and its appearance in the royal houses of Europe gave the disease an air of glamour

unsurpassed in the history of medicine. But there was still no effective treatment to control bleeding or prevent disability. The patient was less likely to fall a victim to blood-letting, but not for another decade could lost blood be safely replaced. Advances were being made towards the relief of other diseases, but the outlook for haemophilia remained uniformly bleak. Thus the seeds of hopelessness became firmly rooted in families where the trait was passed on from generation to generation.

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