REVIEW

How the cholera epidemic of 1831 resulted in a new technique for fluid resuscitation

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Cholera was a much feared disease as it spread across Europe in 1829–1830. The *Lancet* on the 19 November 1831 charted its progress and even published a fold out map of Europe to allow its readers to monitor its approach.[1] The epidemic reached Sunderland in October 1831.

On the 3 December 1831 a Dr W B O'Shaughnessy delivered a lecture to the Westminster Medical Society on the "Blue epidemic cholera", as it was then known. As there was still no known "remote" cause of the disease, he considered it legitimate to look at the effects of the disease and to treat these instead. He had observed that, "universal stagnation of the venous system, and rapid cessation of the arterialisation of the blood, are the earliest, as well as the most characteristic effects."[2] He then posed the question, "What is the best mode by which this artificial arterialisation can be effected ..?" At the time most physicians favoured venesection. Others, "Recommend the inhalation of oxygen gas, or of a mixture of oxygen and atmospheric air, or of the protoxide of azote, ... "laughing gas"..."[2]

He went on, "Now it might rationally be imagined that the success or failure of these methods should afford us a touchstone of some authority, in deciding on the rationality of the principles on which they are practised ..."[2] and concluded that there was some evidence in favour of venesection, if done in time and no other problems were encountered. He found no evidence in favour of oxygenation and conceded that venesection might also fail. In vitro physiology studies had shown that venous blood could be arterialised by agitation in atmospheric air, or contact with highly oxygenised solids or fluids. This led him to suggest the idea of intravenous injection of nitrate or chlorate of potash, "salts which contain the greatest quantity of oxygen". A trial of the technique in a mongrel dog showed that it was safe.

O'Shaughnessy suggested that his method should only be used in patients in extremis. He recommended introducing a small tube, "which should be of gold or ivory" into the external jugular vein, rather than the veins in the ante cubital fossa, because of its proximity to the superior vena cava and because of the reduced risk of air embolism.

Later, O'Shaughnessy analysed the blood from a cholera patient and noted that, "It has lost a large proportion of its water .... it has lost also a great proportion of its neutral saline ingredients".[3] He also recorded that there were only 860 parts water in 1000 parts serum, but made no comment as what was considered normal. A reduction in the water content of blood in a cholera victim was also recorded by W R Clanny in Sunderland.[4] His patient's blood had a water content of only 644 parts per 1000 compared with 765 parts per 1000 in the blood of a sailor (presumably acting as a control). The patient also had an increased proportion of "colouring matter".

By 1832 O'Shaughnessy's work had resulted in a "Report on the chemical pathology of malignant cholera", which was published by the Central Board of Health. The reviewer in the *Lancet* commented that for the treatment of the most severe cases, "the author recommends the injection into the veins of tepid water, holding a solution of the normal salts of the blood; his experiments having, we presume, led him to abandon his former ideas respecting the superiority of highly oxygenated salts for this purpose".[5]

FROM THEORY TO PRACTICE: THE ROLE OF THOMAS LATTA

When the treatment was eventually used in patients normal salts, rather than "highly oxygenised" salts, were used. Thomas Latta, a physician based in Leith, had read O'Shaughnessy's papers in the *Lancet*, and had attempted, unsuccessfully, to remedy the blood deficiencies by the rectal route (a treatment recommended by a Dr Gibson in Newcastle[6]). In his report to the Central Board of Health, dated 23 May 1832, Latta wrote, "I at length resolved to throw the fluid immediately into the circulation. In this, having no precedent to direct me, I proceeded with much caution."[7] His first patient was an "aged female", and he used the basilic vein. The result was remarkable, "Ounce after ounce was injected ... when six pints had been injected, she expressed in a firm voice that she was free from all uneasiness". Unfortunately the patient relapsed and died some hours later, after Latta had left her in the care of the "hospital surgeon". He commented that, "I have no doubt the case would have issued in complete reaction, had the remedy, which already had produced such effect been repeated."

Latta continued, "The apparatus I have used, is a Read's patent syringe, having a small silver tube attached to the extremity of the flexible injecting tube. The syringe must be quite perfect, so as to avoid the risk of injecting air; the saline fluid should never be injected oftener than once into the same orifice, and the vein should be treated with much delicacy to avoid phlebitis." He also warned that great vigilance was needed when using this treatment and listed some reasons for its failure: (1) not enough fluid; (2) underlying disease; and, (3) late application of the remedy.[7]

The *Lancet* dated 2 June 1832, which carried this report also published letters from Drs Robert Lewins, Thomas Craigie, and J Macintosh, in which they described patients with cholera treated with this method. This correspondence concluded with a note written on 2 June by O'Shaughnessy, who wrote that, "The results of the practice described by Drs. Latta and Lewins exceed my most sanguine anticipations".[8]

That the idea of intravenous fluids appealed to some is confirmed by a letter dated 15 June 1832, published in the *Lancet* of 23 June, from a Dr T J Murphy of Liverpool, who claimed to have thought of the idea, "So far back as the 15th of May". He then recounted several cases and collaborations, concluding, "The testimony of the above gentlemen can clearly prove, that the idea had occurred to me prior to its publication, ..."[9] This claim is dismissed by Masson in his biographical essay on Latta.[10]

Further reports of the beneficial effects of this new treatment were published,[11] including this graphic testimonial, "The very remarkable effects of this remedy require to be witnessed to be believed. Shortly after the commencement of

the injection the pulse, which was not perceptible, gradually returns; the eyes, which were sunk and turned upwards, are suddenly brought forward, and the patient looks round as if in health, the natural heat of the body is gradually restored, the tongue and breath, which were in some cases at the temperature of 79 and 80, rise to 88 and 90, and soon become natural, the laborious respiration and oppression of weight of the chest are relieved ... the whole countenance assumes a natural healthy appearance".[12]

However, looking through the pages of the *Lancet* it is clear that intravenous fluid therapy was far from universally accepted. Reports continued to appear of alternative treatments for cholera, such as cold water administration,[13] and salt water emetics.[14] In Manchester tartar emetics were recommended: "The result has been already beyond our expectations, ... We have found it successful in every case during the early stage of incomplete collapse".[15] Langford even went so far as to suggest increasing the dose in advanced disease, but, "If this remedy is not successful, in the most malignant and fatal stage of spasmodic cholera, when the nervous energy is subdued, and the powers of life laid prostrate, it is not wonderful".

In the Parish of St Giles, in London a complicated regimen was adopted including Calomel, powdered rhubarb, compound tincture of rhubarb, castor oil, mucilage of gum arabic, chalk julep, sweet spirits of nitre, and tincture of opium. No mention was made of intravenous fluids, although it did permit the drinking of cold water. Emphasis was placed on warming the patient, putting on a flannel shirt, and going to bed with hot blankets and hot water bottles. Failure of these treatments was ascribed to prior use of stimulants, or failure to maintain external heat.[16]

The idea of intravenous injection was not entirely new, even in 1831. O'Shaughnessy conceded that in 1830 there were reports of Russian soldiers treated for tetanus with intravenous opium.[2] Sir Christopher Wren, as far back as the early 1650s, had performed experiments in which he injected wine and ales into the venous circulation of dogs, with not unexpected results.[17] These experiments prompted attempts at blood transfusion.

A TREATMENT AHEAD OF ITS TIME

The idea of infusing crystalloids, and repeating the infusion as required was new. However, once the epidemic had run its course the treatment seems to have been ignored. The index to volume ii of the *Lancet* 1831–32 contains 29 entries under "Injections venous, in cholera". In the following volume of the Lancet there were none, and in volume ii for 1832–33 there were only two.

Cosnett has suggested a number of reasons for the failure of the treatment to "catch on": (1) it was only used in the moribund, and although some lives were saved it also seemed to accelerate death in others; (2) the treatment was not repeated often enough to maintain fluid balance; (3) the fluid was unsterile (Latta mentions using distilled water), the salts chemically impure, and the solution hypotonic. This resulted in a risk of sepsis, pyrogenic reactions, and haemolysis. "However sound the rationale, the idea was much ahead of contemporary knowledge of physiological chemistry and microbiology."[18]

RE-DISCOVERY

Circulatory physiology caught up some 30 years later, but in mainland Europe, when, in 1864, Goltz suggested that loss of intravascular volume was the cause of death from haemorrhage (rather than the loss of red cells).[19] Fifteen years later, in 1879, while conducting experiments on blood transfusion, Kronecker and Sander found that two dogs haemorrhaged 60% and 50% of their blood volumes respectively could be resuscitated with a warmed solution of 6 g cooking salt and 0.05 g sodium hydroxide in a litre of distilled water given via the external jugular vein.[20] (They also noted that cats did not seem to tolerate such a transfusion). That not just any solution might be effective was demonstrated in 1880 by Drs R Moutard-Martin and Ch Richet who compared the effects of intravenous injection of solutions of sugar and gum. They found that injection of gum increased arterial pressure, while a sugar solution had no effect on blood pressure but caused polyuria.[21]

The practical application of these results was soon realised and in 1881 Bischoff in Basle described using an intra-arterial infusion of a saline solution in a patient with an acute post-partum anaemia.[22] The following year C Egerton Jennings reported his use of a salt solution in the resuscitation of a woman with a severe obstetric haemorrhage.[23] His solution consisted of 20 oz water warmed to 100°F, 50 grains sodium chloride, 3 grains potassium chloride, 25 grains sodium sulphate, 25 grains sodium bicarbonate, 2 grains sodium phosphate, plus 2 drachms absolute alcohol. He also described an infusion kit made to his specification for out of hospital use. This included elastic tubing, cannulas of different sizes, a dissecting kit, and saline powders, so that the infusion solution could be prepared on site. Diagrams of this equipment were published later,[24] and the technique soon repeated.[25]

The following year the *Lancet* reported, "A case in which life was undoubtedly preserved by iv injection of saline fluid .."[26] This referred to a case report in the *Berlin Klinische Wochenschrift*, volume 21, in which a Dr L Szuman described a trauma victim who was anaesthetised with ether, given "artificial respiration" and underwent emergency surgery.[27] However, "As a last effort recourse was had to intravenous injection of a solution of common salt (6 g to1000 g of distilled water) with one gm of sodic bicarbonate". This was achieved by a cut down to the left median vein. The total infusion was of 760 g. Further reports of saline infusions appeared in 1886,[28] 1888,[29] and 1889.[30] At that time it was noted that, "Cases of successful (blood) transfusion are not very common ...",[29] and that, "A simple saline solution is quite as effectual as a mixture of such a solution with defibrinated blood .."[29] W H Brown, who had experience of blood transfusion, advocated the use of saline because, "a supply can be so readily obtained."[30]

ACCEPTANCE OF INTRAVENOUS SALINE RESUSITATION

In 1889 W Hunter delivered three lectures on the physiology, pathology, and practice of transfusion.[31] In the last lecture he commented that the main benefit of blood transfusion was restoration of blood volume and blood pressure, which could just as easily be achieved using saline. By the turn of the century saline transfusion was so important in resuscitation that one eminent surgeon used to tell his students, "No person should die of haemorrhage."[32] Saline was also reported in the treatment of diabetic coma[33] and post-partum haemorrhage.[34] At the same time intravenous injections of serum were also being used.[35] By 1902 saline infusions appear to have become a standard tool in resuscitation, with the addition of "anti-streptococcic serum" in cases of infection or sepsis.[36] The limitations of normal saline became apparent in the first world war and alternatives, such as gum acacia (a 6% solution of gum acacia in 0.9% saline)[37] and hypertonic saline were used[38] in addition to blood. The debate about the ideal resuscitation fluid continues to this day.

Although infusions of saline came of age long after Thomas Latta's death in 1833, Robert Lewins was quite right when he wrote on 18 May 1832, "Verily, Sir, this is an astonishing method of medication, and I predict will lead to wonderful changes and improvements in the practice of medicine."[39]

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