

## THE TREATMENT OF CHOLERA BY INTRAVENOUS SALINE INJECTIONS; WITH PARTICULAR REFERENCE TO THE CONTRIBUTIONS OF DR THOMAS AITCHISON LATTA OF LEITH (1832).

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THE pandemic of cholera, which started from Bengal about 1823, introduced Asiatic cholera to Europe for the first time. It reached Edinburgh early in 1832 from Newcastle, which was attacked towards the end of 1831. From Newcastle it did not spread directly to Edinburgh, but halted for a time at Haddington.<sup>1</sup> The slow rate of spread of the pandemic from Bengal was regulated by the speed of transport, which was chiefly by foot in these days. With increased speed of transport by railways, etc., subsequent pandemics of cholera reached Europe much more quickly.

In Edinburgh and district the epidemic lasted nearly nine months, displaying such a degree of virulence as to destroy in a very short space of time the majority of those attacked.<sup>2</sup> The epidemic could be divided into three phases: (a) From February to 14th June; (b) 15th June to 31st July; (c) 1st August to 1st December. The total number of persons attacked was 1885, and of these, 1065 succumbed. More females than males were attacked.

That the great majority of the medical profession in Great Britain in 1832 were quite unprepared for the treatment of cholera is indicated by the fact that about twenty-four different methods of treatment were advocated. These included, the actual cautery; bastionading the feet; suffocating under a feather bed! The list was humiliating to the profession, but there was at the time much excitement and anxiety amongst medical men, so much so that many lost their reason.<sup>3</sup>

Fortunately, during the epidemic, a very important contribution to the problem of the therapy of cholera, based on sound scientific principles, was made by Dr T. A. Latta of Leith, who is now recognised<sup>4</sup> as the pioneer in the treatment of cholera by intravenous saline injections. That it was courageous therapy at that distant period there can be no doubt, because even at the present time (1944) the Medical Society of London have discussed the difficulties and dangers of intravenous therapy.<sup>5</sup> In addition to the difficulties and dangers of the treatment he also encountered discouraging obstruction from some of his colleagues in carrying it out.

It is remarkable that, so far as can be ascertained, no obituary notices of Latta or of the two colleagues who co-operated with him appeared in any medical journal. To fill the gap the following biographical facts are given regarding Latta and his two colleagues, Mackintosh and Lewins:—

Thomas Aitchison Latta graduated M.D. (Edin.) in 1819 with a thesis, *De Scorbuto*. He resided at 32 Bridge Street in 1822; 1 Sandport Street, 1825; 27 Constitution Street, 1827; 15 Charlotte Street, all in Leith (now incorporated in the City of Edinburgh). He died at the latter residence on 19th October 1833 of consumption "occasioned by his unwearied and unremitting exertions on this occasion (cholera epidemic)." <sup>3</sup> His contributions are dealt with fully later.

John Mackintosh graduated M.D. at Aberdeen University in 1820. After serving in the Ordnance Medical Department he settled in Edinburgh and practised at 31 Albany Street. He lectured in the extramural school on the Practice of Physic and was the author of a book in two volumes on this subject. He was in charge of the cholera hospital at Drummond Street in 1832. He died at Edinburgh on 28th October 1837.

Robert Lewins graduated at Edinburgh in 1813 and became a Fellow of the Royal College of Physicians of Edinburgh on 2nd November 1830. He practised in Leith, where he resided at 6 Quality Street.

Latta adopted the intravenous saline method for the treatment of cholera after reading a report on the analysis of the blood in cholera by O'Shaughnessy.<sup>6</sup> The latter showed that the blood in cholera had lost a large proportion of its water, 1000 parts of cholera blood serum having lost on an average 860 parts of water; it had also lost a great proportion of its neutral saline ingredients; he also noted that all salts deficient in the blood, especially carbonate of soda, were present in large quantity in the peculiar dejecta. Latta<sup>7</sup> had the ability to grasp the implication of these findings and applied the knowledge in his treatment of cholera. He sought to restore the blood of cholera cases to its natural state. At first he tried injecting large quantities of warm water, containing the requisite salts, into the large intestine, and also giving it by mouth. Finding this method and all others to be useless, he resolved to throw the solution direct into the circulation. This he proceeded to do with much caution. He described the solution employed for intravenous injection as artificial serum. It was prepared by saturating water with protoxide of nitrogen holding in solution half a drachm of muriate and eight grains of subcarbonate of soda to the pound (pint) of water. He gives the following account of the first cases treated by him:—

CASE 1. Male, aged 33. In complete collapse stage of cholera. He was given 60 oz. of saline solution intravenously at a temperature of 98° F. Every symptom was permanently removed. No consecutive fever. He was convalescent in four days.

CASE 2. Male, aged 48. Severe case of cholera, seemed hopeless. He had chronic liver and gastric disease. Given seven pints of solution intravenously. This had only a temporary effect. Then given six pints at temperature of 96° F. Next day pulse failed, injection repeated. Fifty hours after first injection he passed urine. Every symptom removed. No consecutive fever.

CASE 3. Female, aged 65. Very advanced case of cholera. Intravenous saline prolonged life, but she died next day.

CASE 4. Male, aged (?). In an advanced stage of cholera. Two pints of saline intravenously at 98° F. only required. There was immediate relief, stools became feculent next morning and he passed urine.

CASE 5. Female, aged 45. Advanced stage of cholera. Two pints of saline intravenously at 97° F. Vomiting and purging stopped. Again given two pints of saline. Stools feculent and she passed urine. She did well.

Latta attached great importance to the use of a vapour-bath to maintain the body temperature as an adjuvant to the intravenous therapy. As we will see, Wall found hot water baths of considerable value as a supplement to intravenous therapy in the treatment of cholera.

*The Lancet*, in a leader<sup>8</sup> on Latta's work, says: ". . . a paper of considerable interest, written by Dr Latta of Leith, detailing several cases of malignant cholera, which, by the intervening agency of the vapour-bath, were successfully treated with saline venous injections at a period of the disease when, without the aid of the auxiliary Dr L. now proposes, the patients would almost certainly have perished. . . . The contrivance is a very good one."

In a further paper,<sup>9</sup> Latta amplifies his account of his method of treatment. He recommends that the temperature of the fluid injected should be 112° F., because 100° F. is too low and produces an extreme sense of cold and rigors; at 115° F. it suddenly excited the heart, the countenance became flushed and great weakness was complained of. He also recommends that the rate of injection should be very slow, not exceeding two to three ounces per minute. The quantity of fluid required will depend on the effect produced, and the repetition of the injection on the demands of the system, which will vary according to the violence of the diarrhœa. The greater the collapse the greater the quantity as a rule. Failure of the treatment is due to (1) quantity of fluid being too small, (2) extensive organic disease, (3) application of treatment too late. The evil of consecutive fever is mitigated by intravenous saline. The apparatus employed by Latta was a Read's patent syringe with a small silver tube attached to the extremity of the flexible injecting tube. The syringe should be in perfect condition to avoid injection of air, the vein should be treated with much delicacy to avoid phlebitis, and injection should never be made more than once at the same orifice.

Lewins, Latta's colleague, in a letter<sup>10</sup> to *The Lancet*, dated 14th June 1832, says: ". . . The failures we have witnessed, in my opinion, afford no real objection to the practice of treating cholera by venous injection—a method of medical treatment which, as I said before, will, I predict, lead to important changes in the practice of medicine, and will entitle Dr Latta's name to be placed amongst the number of those (alas! how few) who have really contributed to the improvement of the healing art."

A very dangerous method of applying Latta's treatment occurred

to Dr T. J. Murphy of Liverpool. He writes:<sup>11</sup> "Having read Dr Latta's paper, my first idea was to return into the system the alvide dejections by injecting them into the venous system; an idea which arose from a quantity having been preserved for my inspection." Fortunately for the patients he was prevented from carrying out the idea by the dejections being seldom preserved. He then prepared an artificial serum as recommended by Latta.

Dr John Mackintosh was in charge of the special cholera hospital in Drummond Street, Edinburgh, during the 1832 epidemic. He gave the intravenous saline treatment an extensive and accurate trial, treating 156 patients by this method. He writes:<sup>3</sup> "The bold idea of restoring the loss at once, by injecting a large quantity of saline solution into the venous system, occurred to the original mind of the late Dr Latta of Leith. . . . He was ably and zealously supported in his investigations by Dr Lewins, who encouraged and assisted him, when others threw every obstacle in the way of his experiments, and too often gave erroneous reports of his practice." Mackintosh used the following solution:—

Sodium chloride . . . . .	half an ounce
Sodium bicarbonate . . . . .	thirty grains
Water . . . . .	Ten pounds (pints)

This solution was in use from 12th May to 21st August 1832, when the quantity of each salt was doubled. The temperature of the fluid was from 106° to 120° F. The solution was strained through chamois leather. Great care in the preparation was recommended. Two persons were employed in the operation, one to open the vein, introduce the tube and keep it in position; the other to take charge of the apparatus and fluid injected. An assistant to be at hand to do anything required, so that the attention of the operators may not be distracted. Care was taken to avoid the introduction of air, and fluid was pumped through the tubes for a few moments. Ten pounds (pints) were introduced in thirty minutes. Mackintosh noted the following effects of the injection: (1) *Pulse*. It was speedily made perceptible after four ounces, good after three pounds (pints). The quantity of fluid injected depended on the state of the pulse. (2) *Cramps*. The effect was quite remarkable, they ceased as soon as pulse improved and seldom recurred. (3) *Temperature*. The effect was almost instantaneous, the body became warm with a gentle and genial perspiration. (4) *Respiration*. This became stronger; sometimes after four pounds it became laboured, but improved with more fluid. (5) *Countenance*. Eyes became prominent, expression animated and mind lively. (6) *Restlessness and uneasy feeling*. This vanished. (7) *Thirst*. This ceased, however urgent. (8) *Secretion of urine*. Soon returned, but in this he was more frequently disappointed than in any other favourable symptom. (9) *Period of death*. This was undoubtedly postponed. (10) *Rigors*. These were almost invariable after the injections. He treated in all one hundred and fifty-six

cases of cholera by intravenous saline and twenty-five recovered. He considered that not one of the cases treated had a chance of recovery by any other means and adds: "We saw no such miracle out of 461 cases (291 deaths) in Drummond Street hospital." He concludes: "Should I ever have charge of cholera patients again, I shall, profiting by the experience I now possess, use the saline solution at an earlier period of the stage of collapse, nay, at its commencement, in order to lessen the thickness of the blood before organic mischief is done. In looking over the cases, my only surprise now is, that one of the individuals recovered by any means that human ingenuity could suggest." He tried the addition of albumin (white of egg) to the fluid to make it resemble the serum of the blood as closely as possible, but he did not find that there was any beneficial effect, so it was laid aside.

In the same year, 1832, as the pioneer work in Leith and Edinburgh was done, a trial was given to the method in the Madras Presidency, particularly by Surgeon John Grant Malcolmson,<sup>12</sup> M.D. (Edin.). He was assistant-surgeon in Madras in 1823, and surgeon in 1832. He treated cases amongst the Madras European Regiment at Secunderabad in 1832. The solution was carbonate and muriate of soda largely diluted in water, and injected into the venous system by means of the ordinary apparatus for blood transfusion. The quantity injected was at first one to two pounds at 98·6° F., subsequently increased to six to eight pounds in some cases. Improvement followed. However, the difficulties of the operation discouraged an extensive trial and apparently it was dropped. J. Macgregor, assistant-surgeon, 39th Foot, in a report<sup>12</sup> on cholera in Bellary, S. India, in April to May 1839, refers to Mackintosh's work on intravenous saline treatment, and says: "I would certainly resort to it in bad cases."

The following incident which occurred at the time, indicated that Latta had not only to contend with the technical difficulties of the treatment, but also with opposition from some of his colleagues. A leader in *The Lancet* of 4th August 1832<sup>13</sup> records that "Dr T. Craigie of Leith wrote a letter published in the *Edinburgh Courant* on 14th June 1832, in which he did not make 'honorable mention' of Dr Latta as the first physician who tried venous injections in cholera, which Dr Latta and his friends considered due from one writing at that particular time and under the existing circumstances. The omission was noticed in an anonymous letter in the *Edinburgh Observer*. This letter contained a remark which Dr Craigie, in a subsequent epistle, spoke of as 'false and unfounded.' The writer of the anonymous letter proved to be Mr John Mitchell, jun., Ship-broker of Leith, who confessed to the authorship for the purpose of demanding an explanation from Dr Craigie as to the above offensive words. An interview took place, casually, in the street, when a trifling assault, with a child's whip, was believed by Dr Craigie to have been committed on him by Mr Mitchell, who is an intimate friend of Dr Latta. The

parties were bound over to keep the peace, although (most unaccountably to the reader) Mr Mitchell denies ('does not admit') that any assault took place, declaring, 'that he had not any whip in his hand when asked for the apology.'” As in the 'index' on the cover of *The Lancet* of 4th August the heading read, "Quarrel between Drs Latta and Craigie," Dr Latta wrote to *The Lancet*<sup>14</sup> as follows: "The quarrel is not mine, but Dr Craigie and Mr Mitchell's, and originated not from any complaint on my part, but in consequence of Dr Craigie applying to a remark made by Mr Mitchell, the offensive term 'utterly false.' As for my name being coupled with venous injections, that is an honour I have not been remarkably fastidious about. The matter is too insignificant for you to revert to, or you would find I did not write to complain of the want of courtesy on this point, but was compelled to come forward in vindication of Mr Mitchell's integrity (who, unknown to me, made the remarks in the *Observer*), and in defence of my own conduct and practice, both of which have been misrepresented in Dr C.'s pamphlet." Dr Mackintosh also refers to Latta's difficulties with his colleagues. He writes:<sup>3</sup> "Few medical men can bear to know that the soundness of their opinions have been questioned: they regard any such attempt as a signal for deadly personal hatred, and view it in the same light as if their moral characters were maliciously assailed."

From the foregoing records it will be apparent that the *odium medicum* was very pronounced, and prevented certain of the profession from recognising a noteworthy addition to therapy.

The next contribution to the treatment of cholera by intravenous saline was made by E. A. Parkes<sup>15</sup> in 1847. He refers to Mackintosh's work. Like Mackintosh he tried the addition of egg albumin to the saline solution. Temperature of solution 98° F. He treated five cases with four deaths, and considered the revivifying effects of the albumin solution seemed to be as well marked as any recorded by the saline solution.

Forty-six years later, in 1893, valuable work on intravenous saline therapy was carried out by A. J. Wall<sup>16</sup> in India. He refers to the work of Latta and Mackintosh. His solution was:

Sod. chloride	. . . . .	four grammes
Sodium carbonate	. . . . .	two grammes
Water	. . . . .	one liter

The temperature of injection was 37° C. Injection made very slowly, not exceeding a liter in twelve minutes. The results of his first series of severe cholera were: out of fifty-eight cases treated, forty-one died, 70 per cent. mortality. In the second series one hundred and thirty-five cases were treated, and ninety-five died, 70 per cent. mortality. He recommended intravenous saline for other conditions in which dehydration was a marked feature. It is also interesting to note that he suggested the addition of gelatine to give more permanent effect to the

solution. He made the important recommendation that rectal temperature in cholera should be taken as a guide to the temperature of the fluid injected. Like Latta he strongly favoured the warm bath for maintaining the body temperature. The range of temperature of the bath being from  $32^{\circ}$  to  $37^{\circ}$  C. The bath to be wheeled to the bedside; the patient, who should not exert himself, is placed in it at full length for from ten to fifteen minutes. It can be repeated again and again. The results are most striking. An important contra-indication is a high rectal temperature,  $103^{\circ}$  F. For hyperthermia he recommends an enema at  $80^{\circ}$  F. or considerably below this. In less severe cases he advised subcutaneous instead of intravenous injection of saline. The solution for this purpose should contain no alkali or anything that can cause the least irritation.

The next advance in intravenous saline therapy was made by Sir Leonard Rogers<sup>17</sup> in Calcutta between 1906 and 1915. He worked out his well-known standard method of treatment for cholera, which is now generally employed. By a simple clinical method the specific gravity of the blood is estimated, and the necessity of an intravenous saline injection can be ascertained before the patient has entered the stage of collapse, and it also gives an indication of the quantity of fluid required. He employed hypertonic saline, using two solutions; the first containing sodium chloride one hundred and twenty grains, and calcium chloride four grains to one pint of water. The second contains sodium chloride ninety grains, sodium bicarbonate one hundred and sixty grains to one pint of water. If four pints are required, then one pint of the alkali solution is given, followed by three of the hypertonic saline. He showed the importance of taking the rectal temperature. To avoid consecutive hyperpyrexia the temperature of the solution should not be above  $80^{\circ}$  F., if the rectal temperature is found to be above  $101^{\circ}$  F. Temperature of fluid should not exceed  $98^{\circ}$  F., except when the rectal temperature is below normal, then the temperature of the solution may be two to three degrees above  $98^{\circ}$  F. By the use of his scheme of treatment a striking reduction in deaths from cholera in hospital cases was brought about.

Recently Wilkinson,<sup>18</sup> from his experience of cholera in Hongkong, has expressed a preference for normal, instead of hypertonic saline, for intravenous therapy, because hypertonic saline injections were not found successful there during the epidemic in 1931, judging by mortality; also, theoretically, the main effect of hypertonic saline intravenously is to induce a flow of fluid into the blood stream, and the only place in the body which could yield it would be the gut, and this would mean in cholera more toxin absorbed from the gut, and more violent subsequent reactions.

From the above summary it will be seen that intravenous injection of saline solution is considered an essential method of treatment of cholera at the present time, and that Latta, in 1832, had the great merit of being the first to employ it in cholera. His treatment was not

empirical, but based on sound scientific observations. As would be expected the early technique was primitive, but the method has undergone progressive evolution and improvement; however this does not detract in the slightest degree from his bold and original conception. Looking at the technique with the advantage of present-day knowledge is interesting. For example, we see that the temperature of the fluid injected was too high, and might easily produce dangerous hyperpyrexia. Further, the injections were commenced at a very advanced and almost hopeless stage of the disease; this was clearly recognised by both Latta and Mackintosh in their reflections on the results after the cessation of the epidemic, and they rightly concluded that a very considerable improvement in the mortality rate would have been effected if the injections had been started much earlier.

From what has been stated in this paper, the importance of the work of Latta and his colleagues, as the pioneers of intravenous saline treatment of cholera, will be realised, and it is hoped that the statement will give them the place they deserve in medical history, and keep their memory green.

The wisdom that they taught us  
Is proven prophesy.

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