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The death of Charlotte Brontë from hyperemesis gravidarum and refeeding syndrome: A new perspective

Simon P. Allison, Dileep N. Lobo

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1 2	Short Communication			
2 3 4 5	The death of Charlotte Brontë from hyperemesis gravidarum and refeeding syndrome: A new perspective			
5 6 7	Simon P Allison ¹			
7 8 9	Dileep N Lobo ^{2,3}			
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11 12 13	¹ Formerly Consultant Physician and Professor of Clinical Nutrition, Nottingham University Hospitals NHS Trust and University of Nottingham, Queen's Medical Centre, Nottingham NG7 2UH, UK			
14 15 16 17	² Gastrointestinal Surgery, Nottingham Digestive Diseases Centre and National Institute for Health Research (NIHR) Nottingham Biomedical Research Centre, Nottingham University Hospitals NHS Trust and University of Nottingham, Queen's Medical Centre, Nottingham NG7 2UH, UK			
18 19 20	³ MRC/ARUK Centre for Musculoskeletal Ageing Research, School of Life Sciences, University of Nottingham, Queen's Medical Centre, Nottingham NG7 2UK, UK			
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31	Address for correspondence:			
32	Professor Dileep N Lobo			
33	Gastrointestinal Surgery			
34	Nottingham Digestive Diseases Centre			
35	Nottingham University Hospitals NHS Trust and University of Nottingham			
36	E Floor, West Block			
37	Queen's Medical Centre			
38	Nottingham NG7 2UH, UK			
39	Tel: +44-115-8231149			
40	Fax: +44-115-8231160			
41	E-mail: <u>Dileep.Lobo@nottingham.ac.uk</u>			
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44 Abstract

45 Many theories have been advanced concerning the cause of Charlotte Bronte's death, none of 46 which fully explain all the symptoms she experienced in the course of her final illness. Her 47 death certificate records the cause of death as phthisis (tuberculosis), but there is no evidence, 48 other than circumstantial, to support this diagnosis. A diagnosis of Addison's disease, caused 49 by tuberculosis of the adrenals, has been proposed, but this is unlikely, since it does not fit 50 well with two and a half months of severe anorexia, nausea and vomiting, followed by 51 remission of these symptoms and eventual death. We agree, as suggested by some authors, 52 that the most likely diagnosis was hyperemesis gravidarum, but suggest that this was 53 complicated by the refeeding syndrome consequent on recovery of her appetite after 54 resolution of hyperemesis gravidarum and that this was the cause of her death. These two 55 diagnoses are compatible with the remission in her symptoms of anorexia, nausea and 56 vomiting in the third week of March 1855, followed by further decline and death.

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59 Many theories have been advanced concerning the cause of Charlotte Bronte's death, none of 60 which fully explain all the symptoms she experienced in the course of her final illness as described in a contemporary account [1] and in more recent publications. [2-6] 61 On June 29th 1854 she married Arthur Nicholls, her father's curate, and by all accounts, 62 63 including her own, it was a very happy relationship. In November of that year, following a long walk in the rain, she developed a chill, which some have suggested, contributed to her 64 final illness, but this seems unlikely since she appears to have largely recovered from it by the 65 end of the year. Mrs. Gaskell, her contemporary biographer, records that, at the beginning of 66 67 January 1855, Charlotte "was attacked by new sensations of perpetual nausea and ever recurring faintness". [1] A doctor "assigned a natural cause (i.e. pregnancy) for her miserable 68 indisposition" and said that it would soon pass. [1] Mrs. Gaskell then writes, "the dreadful 69 sickness increased and increased, till the very sight of food occasioned nausea". She records 70 one witness as saying, "a wren would have starved on what she ate during those last six 71 72 weeks". [1] From mid-January she suffered from nearly continuous vomiting and took to her bed, too weak to sit up. Her biographer goes on to record, "About the third week in March 73 74 there was a change; a low wandering delirium came on, and in it she begged constantly for 75 food and even for stimulants. She swallowed eagerly, but it was too late." [1] She died On March 31st 1855, Reading Mrs. Gaskell's account, we were particularly struck by this 76 description of her last few days, which we have put in italics, as it seemed to us to negate 77 78 nearly all the suggested diagnoses and to be the crucial clue to a diagnosis, which hitherto has 79 been overlooked.

Her death certificate records the cause of death as phthisis (tuberculosis), but there is no evidence, other than circumstantial, to support this diagnosis. It was a common debilitating and fatal illness at the time, and her siblings Maria, Emily, Anne, and Branwell all died of it after prolonged illness. However, in a letter to a friend, three months after her marriage, she

84 wrote, "We are all pretty well, and for my own part, it is long since I have known such 85 comparative immunity from headache, &c." [1] She reported no cough, and the symptoms of two and a half months of nausea and vomiting, followed by remission and recovery of 86 87 appetite, hardly fit tuberculosis or any of the other suggested infectious illnesses such as 88 typhus or typhoid. One author [7] has proposed a diagnosis of Addison's disease caused by 89 tuberculosis of the adrenals. We consider this unlikely, since it does not fit well with two and a half months of severe anorexia, nausea and vomiting, followed by remission of these 90 91 symptoms and eventual death. Symptoms of such severity can occur in Addisonian crisis but 92 would have been fatal in a much shorter time and would not have remitted spontaneously. The one diagnosis which fits all the features of her illness between January and March, ending 93 94 in spontaneous remission of symptoms in the third week in March, is hyperemesis gravidarum 95 as suggested by Channing in 1857 [8] and Rhodes in 1972 [9] and discussed by Fitzgerald in 96 1979 [10] and by Coad and colleagues in 2002. [11] We are puzzled by suggestions that pregnancy was unlikely. [7] She had been married for six months, the doctor who examined 97 98 her thought she was pregnant, and there are accounts of conversations with her servant 99 Martha Brown, in which the forthcoming child was mentioned. [1] Nausea and 'morning 100 sickness' are also common features of the first trimester of pregnancy, although symptoms of 101 the severity and duration described in Charlotte's case occur in only 1% of pregnancies and 102 nowadays are treated with parenteral or enteral nutrition, anti-emetics, and intravenous fluid 103 and electrolytes, none of which were available in Charlotte's time.

By the third week in March, Charlotte had lost a great deal of weight and would have been malnourished, with deficiencies of protein, energy, vitamins and minerals. She would also have been in negative salt and water balance, causing a postural fall in blood pressure and faintness: gastric acid loss would have led to an hypochloremic alkalosis, and potassium deficiency as her kidneys tried to correct the alkalosis by reabsorbing hydrogen ions in

109	exchange for potassium. These effects of her hyperemesis gravidarum would have been
110	serious in themselves, but they created an even greater risk of the refeeding syndrome, once
111	she was able eat again. This syndrome, [12] which can occur with oral or with artificial
112	refeeding was first described at the end of the second world war among malnourished
113	concentration camp survivors who were refed too rapidly with, in many instances, fatal
114	consequences. [13, 14] It was also described by Majumdar and Dada [15] in a patient with
115	hyperemesis gravidarum who would almost certainly have died without modern treatment. Its
116	features include:

117 Hypophosphatemia, as the cells take up glucose, which increases the demands on 118 phosphate reserves for phosphorylation and ATP synthesis. This causes muscle and 119 cardiac weakness, respiratory depression, delirium, coma, and death in severe cases. Hypokalemia, due to the action of insulin and glucose on cell membranes and the 120 121 increased cellular uptake of potassium as new glycogen and protein are formed. 122 Hypokalemia leads to muscle weakness and cardiac arrhythmias and would have been 123 a particular risk in a case like Charlotte's where, due to hyperemesis, hypokalemic 124 alkalosis was already present at the time of refeeding.

• Hypomagnesemia.

Thiamine (vitamin B1) deficiency, as depleted stores of this vitamin, an essential
cofactor in glucose metabolism, are used up. This leads to irreversible nervous system
damage (Wernicke's encephalopathy).

Although, after a lapse of 163 years since Charlotte Bronte's death, uncertainties must inevitably remain, we suggest that the diagnoses which most closely agree with the recorded clinical features of her last illness are hyperemesis gravidarum complicated by the refeeding syndrome. In particular, these diagnoses are compatible with the remission in her symptoms

- 133 of anorexia, nausea and vomiting in the third week of March 1855, followed by further
- 134 decline and death on March 31^{st} .

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164 165 Author contributions

- 166 167 Both authors contributed equally to the manuscript.