British Journal of Psychiatry (1988), **153**, 72–75

Physical Complications in Anorexia Nervosa

Haematological and Neuromuscular Changes in 12 Patients

E. SHUR, R. ALLOWAY, R. OBRECHT and G. F. M. RUSSELL

Of twelve patients consecutively admitted to the Maudsley Hospital Eating Disorders Unit, four had neuromuscular abnormality, eight haematological abnormality, and four no abnormality. All those having neuromuscular signs had concomitant haematological dysfunction. Vomiting, and food restriction with vegetarianism, appeared more likely to lead to complications than either food restriction alone or laxative abuse. The physical status of severely underweight patients admitted for refeeding needs to be carefully monitored.

The Maudsley Hospital Eating Disorder Unit admits severely ill patients for treatment, yet despite often-extreme cachexia, serious physical complications are remarkably rare. The occasional occurrence of physical decompensation in such patients requires vigilance, and we have reported (Alloway *et al*, 1985) severe neuropathy and myopathy occurring in two patients admitted to the Unit. As there might be underreporting of such physical complications, the neuromuscular and haematological functions in patients consecutively admitted for refeeding were examined.

Haematological changes in anorexia nervosa have been previously described, and include hypocellularity of the bone marrow with accumulation of mucopolysaccharide material, and peripheral pancytopenia with morphological abnormalities of erythrocytes. The abnormalities are usually promptly reversed by weight gain (Mant & Faragher, 1972; Warren & van de Wiele, 1973; Rieger *et al*, 1978; Amrein *et al*, 1979). Garfinkel & Garner (1982) reviewed the literature and reported transient haematological dysfunction to be common in anorexia nervosa. It is probably a non-specific effect of malnutrition, since studies from Europe during World War II (Beattie, 1948; Szejnman, 1979) also showed a high frequency of blood-cell aplasia in malnourished individuals.

On the other hand, studies of neuromuscular function in anorexia nervosa have been few, although 19th-century authors noted paradoxical overactivity in severely wasted patients. In 1874, Gull wrote "for it seemed hardly possible that a body so wasted could undergo the exercise so agreeable" and Laségue (1873*a*) remarked "far from muscular power being diminished, this abstinence tends to increase the aptitude for movement". More recently, Bliss & Branch (1960) reported muscular weakness in energetic anorectic patients. This occurred below a critical weight and appeared to be a function of the rate of weight loss. Lindboë *et al* (1982) and Slettebø *et al* (1984) carried out muscle biopsies in weak anorectic patients and reported a type of histological change associated with cachexia (type 2-fibre atrophy) as opposed to muscle-fibre atrophy secondary to denervation (which produces both type 1- and type 2-fibre atrophy). This suggests that the muscle pathology in cachexia is a primary phenomenon, although the pathophysiology is not well understood (Weller, 1984). This study assessed the rates of these complications in our patients, and searched for patient characteristics that might predict physical decompensation.

Method

Twelve patients consecutively admitted to the Maudsley Hospital Eating Disorders Unit were examined for signs of haematological and neuromuscular dysfunction. Patients 1 and 12 were the subjects of a previous publication (Alloway *et al*, 1985). Patients were assessed by a full physical examination, paying particular attention to neurological and motor function. Muscle power was assessed on proximal- and distal-muscle groups, using a 5-point scale, and electromyograms (EMGs) were performed during the first week of admission on proximal and distal muscles of the upper and lower limbs. Conventional concentric needle EMGs were performed using an MS-6 Medelec electromyograph, applying Payan's method for the study of motor units. Muscle biopsy was performed on one patient (case 12, Table I) from the left quadriceps muscle. Blood investigations included full blood counts, ESR, and measurement of levels of urea and electrolytes, calcium and phosphate, creatine kinase, vitamin B_{12}, folate, iron, and total iron-binding capacity, and thyroxine (T4).

Of the 12 patients, 11 were female and one (case 12) male. Eleven fulfilled the criteria for anorexia nervosa (Russell, 1970). One patient fulfilled the criteria for bulimia nervosa (Russell, 1979). Details of the patients' ages, degrees

TABLE I
Patient characteristics, neuromuscular and haematological abnormalities

Patient's case number	*Age (years)*	*Sex*	*Admission weight (kg)*	*Percentage weight loss*	*Duration of illness (years)*	*Method of weight loss/ duration (years)*	*Neuromuscular abnormality*	*Haematological abnormality*
1	17	F	35.6	37.5	1.8	E, B+V/1.6	+	+
2	20	F	30	36.9	2.0	E, V, L/1.5	−	+
3	17	F	34.1	31.8	4.0	E, R/1	−	−
4	24	F	35.5	31.7	11	V/1.5	+	+
5	23	F	35.9	29.6	2	E, R/2	−	−[1]
6	33	F	44.5	17.6	17	E, L/6	−	−
7	34	F	34	35.8	3	E, L/1	−	−
8	22	F	31.7	36.6	7	R, Veg/7	+	+
9	20	F	32.7	34.6	5	R/1	−	+
10	21	F	37	35.1	1.1	E, R/0.2	−	+
11	18	F	41.9	26.5	2	E, R/2	−	+
12	16	M	40.8	39.1	2	E, R, Veg/2	+	+

R = dietary restriction; V = vomiting; L = laxative abuse; B + V = bingeing and vomiting; Veg = vegetarian; E = excessive exercise.
1. This patient had a lymphocytosis which was not considered to be directly related to her eating disorder.

of weight loss, durations of illness, and methods used to induce weight loss are shown in Table I. Patients were usually young females with severe weight loss, and many had had previous admissions for treatment, indicating that they were a selected population of severely ill patients. Most exercised excessively, and rates of self-induced vomiting and laxative abuse were high. Two patients (cases 8 and 12) were vegetarian.

Results

Neuromuscular and haematological abnormalities related to illness behaviour, body weight, and duration of illness are shown in Table I. Four patients showed abnormal neuromuscular function (defined as significant muscular weakness on clinical examination together with either an abnormal EMG and/or raised creatine kinase or an abnormal muscle biopsy). Case 1 involved the most severely affected patient, who had gross proximal-muscle weakness, absent or diminished tendon reflexes, and a creatine kinase level of 638 IU/litre. Her EMG showed evidence of both reduced nerve conduction rate and muscle dysfunction, suggesting a mixed myopathic and neuropathic disorder. On refeeding, she became temporarily paralysed and developed cardiac failure, which resolved after 2 weeks, with a return of muscle power. During this period, her serum potassium varied between 3.4 and 3.8 mmol/litre. Case 4 involved muscular weakness with raised creatine kinase (163 IU/litre) and an EMG suggesting myopathic changes. Patient 8 had muscle weakness and a myopathic picture on EMG, but her creatine kinase level was normal. In case 12, the patient had severe upper-limb weakness in a proximal distribution, which was confirmed on the EMG. Her plasma-creatine kinase level was normal, but a muscle biopsy revealed both type 1- and type 2 fibre atrophy, with type 2 fibres being most severely affected (virtually all atrophic). This predominance of type 2-fibre atrophy suggests a primary myopathic component, and not a change secondary to neuropathy. There was no evidence of necrosis, inflammatory infiltrates, or loss of fibres, making an infection or prolonged denervation atrophy unlikely. These findings suggest that the muscular weakness observed in our patients was due to a primary proximal myopathy.

It is noteworthy that all patients with muscular weakness either chronically induced vomiting, or were vegetarian, although one patient who induced vomiting (case 2) did not show muscular weakness. Patients with muscular pathology usually had severe weight loss (a loss of between 32% and 39% of healthy body weight). In no case was muscular weakness associated with electrolyte abnormalities. In case 1, there was a transient reduction in the patient's potassium level on day six (3.4 mmol/litre), but on other days the levels were within the normal range. No other patients with muscular weakness had low plasma-potassium levels. On the other hand, in cases 5, 6, and 11, patients had reduced plasma-potassium levels (3.3, 3.3, and 3.5 mmol/litre respectively), but did not show muscle weakness.

Six patients had reduced plasma-urea levels (range 1.7–2.7, normal range 3.3–6.6 mmol/litre), probably as a result of protein deficiency. In every case plasma-vitamin B_{12} and -folate levels were within normal limits. Seven of 12 patients showed haematological abnormalities (Table II) consisting of either anaemia, leucopenia, or thrombocytopenia, or combinations of these. One patient (case 5) had a lymphocytosis. All four patients who showed neuromuscular abnormalities also had haematological changes. Often anaemia did not appear until the second or third week. In case 1, the patient's haemoglobin level fell to 8.4 g/dl during the second week of admission. Both she and patient 12 showed a diffuse purpuric rash, which was associated with thrombocytopenia. Spontaneous recovery of blood elements usually occurred, although leukopenia often persisted for several weeks. There were no clear patient characteristics associated with haematological dysfunction.

https://doi.org/10.1192/bjp.153.1.72 Published online by Cambridge University Press

TABLE II
Haematological abnormalities on admission

Patient's case number	*Hb: g/dl*	*WBC: mm^{-3}*	*Platelets: mm^{-3}*	*White cells*
1	12.1	7100	40 000	Lymphopenia
2	13.9	4200	N	Neutropenia
4	12.8	4200	N	Lymphopenia
5	13.9	9800	N	Lymphocytosis[1]
8	12.8	3600	N	Leucopenia
9	13.0	4400	N	Neutropenia
10	11.4	2800	N	Leucopenia
11	12.5	2400	N	Leucopenia
12	14.7	5700	123 000	Leucopenia

N = normal; Hb = haemoglobin; WBC = white blood cells.
1. This was not considered to be directly related to the eating disorder.

Discussion

The high rates of neuromuscular and haematological abnormalities seen in our sample may be explained by the fact that the selection process on referral to our unit resulted in the sample being biased towards severely ill cases. In severely ill patients admitted to hospital for treatment of anorexia nervosa, such complications may be more common than had previously been believed.

Haematological changes have been previously described in anorexia nervosa (Mant & Faragher, 1972; Rieger *et al*, 1978; Amrein *et al*, 1979; Ledingham, 1986). Mild anaemia, neutropenia, and thrombocytopenia are common, and the bone marrow is hypocellular, with the deposition of mucopolysaccharide substances. Changes in red-cell morphology occur frequently, particularly the presence of spur cells. Reversal of these changes occurs with refeeding, and they are not usually of clinical significance. Mant & Faragher (1972) have suggested that the haematological changes are due either to subclinical deficiency of iron or folic acid, or to changes in plasma volume. The latter explanation would not account for the bone-marrow changes, nor the changes in red-cell morphology, and it is likely that protein–energy malnutrition *per se* may have a deleterious effect on haematopoiesis. Similar haematological findings have been described in patients with malnutrition due to other causes, e.g. Beattie (1948) described bone-marrow aplasia and pancytopenia in malnourished subjects in The Netherlands during the Second World War even in the absence of vitamin deficiency. The haematological abnormalities found in eight of our twelve patients are consistent with these reports.

On the other hand, the type of neuropathic and myopathic changes found in four of our twelve patients was unusual. The two most severely ill patients had evidence of both neuropathy and myopathy, while the other two affected had only myopathic changes. In all four cases, the myopathy exceeded the neuropathy, and the latter was only present in the most severe cases. This is in contrast to the changes found in underdeveloped countries, where malnutrition leads predominantly to a neuropathy with a secondary myopathy (Dastur *et al*, 1979). The finding of a myopathy preceding a neuropathy is unusual, and may be a feature peculiar to severe anorexia nervosa. The causes of the myopathic and neuropathic abnormalities could include vitamin deficiency, electrolyte imbalance, protein–energy malnutrition, or combinations of these. Hysterical weakness also needs to be considered. Electrolyte imbalance, in particular hypokalaemia, was not severe enough to explain the findings in case 1 and was not present in the other three cases. Hysterical weakness was ruled out immediately in view of the clear evidence of muscle dysfunction: the proximal limb-girdle distribution of weakness and wasting, the absence of tendon reflexes, and the EMG and plasma-creatine kinase abnormalities. It may be that excessive exercise in the presence of chronic protein–energy malnutrition predisposes to myopathic changes. The fact that myopathy was associated with either self-induced vomiting or a vegetarian diet, but not laxative abuse, is a further pointer to the primary role of undernutrition in causing this complication.

It is unclear why neither neuromuscular nor the above-mentioned haematological abnormalities occurred in any of cases 3, 5, 6, and 7. Although two of the patients abused laxatives, none induced vomiting. Vomiting, and dietary restriction with vegetarianism, seemed to be more detrimental than laxative abuse, or dietary restriction, alone. The combination of peripheral neuropathy and congestive cardiac failure occurring in case 1, soon after refeeding had begun, points to a diagnosis of thiamine deficiency. Perhaps a combination of chronic self-induced vomiting and poor diet can produce thiamine deficiency. A case of thiamine deficiency secondary to anorexia nervosa was described by Handler & Perkin (1982). It is suggested that measures of thiamine function be carried out in severely ill patients. In addition, refeeding should be gradual, in order not to present a sudden carbohydrate load, which can precipitate beri-beri in thiamine-deficient patients.

In conclusion, protein–energy malnutrition was probably the source of the dysfunction seen in our patients. In the more severely ill patients, thiamine

deficiency may have contributed. In spite of severe complications in some patients, all made a complete physical recovery. Nonetheless, the physical status of severely underweight patients admitted for refeeding needs to be carefully monitored.

References

ALLOWAY, R., REYNOLDS, E. H. & RUSSELL, G. F. M. (1985) Neuropathy and myopathy in two patients with anorexia and bulimia nervosa. *Journal of Neurology, Neurosurgery and Psychiatry*, **48**, 1015–1020.

AMREIN, P. C., FRIEDMAN, R., KOSINSKI, K. & ELLMAN, L. (1979) Haematological changes in anorexia nervosa. *Journal of the American Medical Association*, **241**, 2190–2191.

BLISS, E. C. & BRANCH, C. M. M. (1960) *Anorexia Nervosa*. New York: PB Hoebner Inc.

BEATTIE, J. (1948) In *Malnutrition and Starvation in the Western Netherlands, September 1944–July 1945*. (eds G. C. E. Burger, J. C. Drummond & H. R. Stanstead). The Netherlands: The Hague General State Printing Office.

DASTUR, D. K., DAVER, S. M. & MANGHAN, D. K. (1979) Changes in muscle in human malnutrition with an emphasis on the fine structure in protein calorie malnutrition. In *Progress in Neuropathology* (ed. H. H. Zimmerman), vol. 5. New York: Raven Press.

GARFINKEL, P. E. & GARNER, D. M. (1982) *Anorexia Nervosa, a Multidimentional Perspective*. New York: Brunner/Mazel.

GULL, W. W. (1874) Anorexia nervosa (Apepsia hysterica, Anorexia hysterica). *Transactions of the Clinical Society of London*, **7**, 22.

HANDLER, C. E. & PERKIN, G. D. (1982) Anorexia nervosa and Wernicke's encephalopathy: an undiagnosed association. *The Lancet*, *ii*, 771–772.

LASÉGUE, E. C. (1873*a*) De l'anorexie hysterique. *Archives of General Medicine*, **1**, 385.

—— (1873*b*). On hysterical anorexia. *Medical Times*, **2**, 265.

LEDINGHAM, J. G. G. (1986) In *Oxford Textbook of Medicine* (2nd edn) (eds D. J. Wetherall, J. G. G. Ledingham & D. A. Warrell) vol.1, pp. 8–34. Oxford: Oxford University Press.

LINDBOË, C. F., ASKEROID, F. & SLETTEBØ, M. (1982) Muscle changes in skeletal muscles of young women with anorexia nervosa. *Acta Neurolopathologica*, **56**, 299–302.

MANT, M. J. & FARAGHER, B. S. (1972) The haematology of anorexia nervosa. *British Journal of Haematology*, **23**, 737–749.

RIEGER, W., BRADY, J. P. & WEISBURG, E. (1978) Haematological changes in anorexia nervosa. *American Journal of Psychiatry*, **135**, 984–985.

RUSSELL, G. F. M. (1970) Anorexia nervosa, its identity as an illness and its treatment. In *Modern Trends in Psychological Medicine* (2nd edn) (ed J. H. Price). London: Butterworths.

—— (1979) Bulimia nervosa: an omnious variant of anorexia nervosa. *Psychological Medicine*, **9**, 429–448.

SLETTEBØ, M., LINDBOË, C. F. & ASKEVOLD, F. (1984) The neuromuscular system in patients with anorexia nervosa. *Clinical Neuropathology*, **3**, 217–224.

SZEJNMAN, M. (1979) In *Current Concepts in Nutrition*, vol. 7 (ed M. Winick) (pp. 161–187). New York: Wiley.

WARREN, M. P. & VAN DE WIELE, R. L. (1973) Clinical and metabolic features of anorexia nervosa. *American Journal of Obstetrics and Gynaecology*, **117**, 435–449.

WELLER, R. O. (1984) Diseases of muscle. In *Colour Atlas of Neuropathology*, Ch. 15, p. 162. Oxford: Oxford University Press.

*E. Shur, MBBCh, MPhil, MRCPsych, *Senior Lecturer in Psychiatry and Honorary Consultant Psychiatrist, Queen Mary's Hospital and Westminster Hospital Medical School*; R. Alloway, MA, MBBS, MRCPsych, *Senior Registrar in Psychiatry*; R. Obrecht, MD, *Consultant Neurophysiologist, Maudsley Hospital*; G. F. M. Russell, MD, FRCP, FRCP(Ed), FRCPsych, *Professor of Psychiatry, Institute of Psychiatry and Maudsley Hospital*

*Correspondence: *Queen Mary's University Hospital, Roehampton Lane, London SW15 5PN*