Section of Medicine

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DISCUSSION ON ANOREXIA NERVOSA

Professor John A. Ryle: Whether we can conclude from the increased output of papers bearing on the subject of anorexia nervosa that the incidence of the malady itself has risen or merely that it is receiving more frequent recognition and closer study I cannot say. When I last reviewed my material in 1936, it included 55 private cases seen within a period of thirteen years. Since then, I have seen a further eight cases in private practice and three or four others under the care of colleagues at Addenbrooke's Hospital. The maximum number of private cases seen by me in any one of the last fifteen years was 12 (in 1932), the minimum one (in 1927 and 1937), and the average four. Excepting that 19 cases were referred to me during 1931 and 1932, my own experience does not suggest a recent fluctuation in incidence. Reading the case histories I could discover no common factor to explain the higher figures in those two years. The spread of the slimming fashion, now happily on the wane, and the more emotional lives of the younger generation since the War might have been expected to provide a general increase, but these influences may well have been counteracted by the growth of a healthy athleticism among girls and young women and the greater freedom from restraints which they now enjoy.

Historical

So far as the history and literature of anorexia nervosa are concerned we should remind ourselves that Richard Morton [10] described an indisputable case in his little book on Phthisis in 1694; that Thomas Hobbes, the philosopher, gave an account of his visit to a case which was quoted by Samuel Gee [8], who himself gave a concise picture of the disorder under the title of "nervous atrophy" in his well-known Medical Lectures and Clinical Aphorisms; and that Clifford Allbutt [2], Lockhart Stephens [14], Hurst [9], Venables [15], Conybeare [4], Allison and Picton Davies [1], Ross [11], and Sheldon [13], in this country, have made notable contributions to the subject, which was also chosen by me for the Schorstein Memorial Lecture [12] in 1936. The best account in the French literature is probably that of Déjerine and Gauckler [5]. Abroad there has clearly been confusion of late years between anorexia nervosa and the organic syndrome of pituitary cachexia or Simmonds' disease. Over and above all other descriptions, however, we must still hold Gull's [7] and [8] portraiture of the malady (now 70 years old) in highest esteem, and to him we owe both the name, which I have shown good reasons for retaining, and the generally accepted view that the anorexia and its associations and consequences depend upon a morbid mental state.

Ætiology

According to my observations, 90% of the cases are in women, and of these 70% are in girls and young women below the age of 30. Of these, nearly all are unmarried. My youngest patient was aged 14½. The average age in the youthful female group was 20. In my older female group the ages ranged from 31 to 59, the average age being 44. The ages in the male group ranged from 19 to 34, with an average age of 25.

The majority of cases may be classified as psycho-neurotic, but there are borderline and graver cases which might be classified, as Ross has suggested, as anorexia

psychotica. The adjective " nervosa " is, however, sufficiently comprehensive to include both groups. Dr. C. P. Symonds has suggested to me that in a certain proportion of cases the nervous anorexia is an early manifestation of cyclothymia. We need a more careful analysis of family histories and after-histories than has yet been available to support this view, which I am nevertheless inclined to accept. It should be remembered that a family history of a depressive psychosis does not exclude the possibility of other coincident nervous traits, and an ill-defined nervous heredity is common in anorexia nervosa. The emotional instabilities of young adult life play an important part in ætiology. Of initiating or contributory factors, other than slimming in response to teasing on the score of adolescent plumpness (and this can rarely be accepted as a sole cause), love affairs, broken engagements, school attachments and jealousies, home sickness (especially in the case of girls sent abroad), unhappy home life, spoiling by devoted parents, mental shocks, examinations and overwork, and convalescence from a physical illness or operation are all noteworthy.

Perpetuating factors include morbid enjoyment of the interest and anxiety aroused by the illness, the sense of power over the mother obtained thereby, and a temperamental (or maybe symptomatic) exaggeration of the sense of duty with which there are often associated a restless activity and a tendency to the performance of good works and fussy actions on behalf of others. Although they may be " devoted to each other " mother and daughter are frequently " at loggerheads " or " on each other's nerves ". The lack of a diagnosis must also be accepted as a common perpetuating factor.

Physical illness and operation and menopausal ill-health would seem more frequently to provide the background for the malady in patients of the older group.

Clinical Picture

The clinical picture of the fully developed case (and we should remember that the earlier stages too often pass unrecognized) is that of a young woman presenting the appearance of more or less advanced starvation. The bony points are prominent. The abdomen is scaphoid. The face is thin but the colour is usually retained. There is a fine downy hirsuties on the cheeks, the forearms, and the back. On the abdomen the hair often shows the male distribution. The pulse is slow, the blood-pressure low—often 100 mm. (systolic) or below—and the temperature is subnormal. The loss of weight may be anything from 1 to 4 st. Amenorrhœa is nearly constant. Emotional derangement in the form of moodiness, tantrums, or tears, is not far to seek and is usually reported by the mother, although the patient may appear natural and even cheerful at a first interview. Subterfuge in the disposal of food and concealed vomiting may create difficulties and call for careful watching. In contrast with these striking physical findings and in spite of extremely inadequate diets there is rarely any evidence of anæmia or deficiency disease. A degree of activity of mind and body which would be impossible in the presence of emaciation due to any of the organic wasting diseases is often remarked, but is not invariable. Diagnosis should not be difficult. In the words of Déjerine and Gauckler [5] " Or le diagnostic de l'anorexie mentale est extrêment simple ; il suffit d'y songer." I do not believe that there should as a rule be any serious difficulty in differentiation from Simmonds' disease, which is a rare condition, but this aspect of the subject I shall leave to Dr. Sheldon and Dr. Spence. Bruckner, Wies and Lavietes [3] have recently considered the difficulties in differentiation which may arise and have carefully studied the distinctive features.

Prognosis

Both Ross [11] and Venables [15] have shown that with sensible institutional treatment the prognosis of anorexia nervosa in young women is almost uniformly good. The younger the patient in my experience the better the result, partly, perhaps,

because the diagnosis is more quickly made, partly because the psychological disturbance is usually of simpler type, and partly, maybe, through the natural resilience of childhood. Home treatment is commonly unsatisfactory on account of the mother-daughter relationship. Nevertheless, approximately one half of my cases did well with home treatment. In cases of long standing, treatment is less easy and prognosis less certainly happy. A few cases recover incompletely to the extent that the restoration of weight and appetite are only partial, amenorrhœa persists, and the young woman remains " difficult " and " different " through life. The fatal cases have commonly been diagnosed late and treated inadequately. Some of them should probably come within the psychotic group. Among the 37 cases (out of 55) which were followed up in the series reported in my Schorstein Lecture there were four deaths. The causes of death include simple starvation and starvation complicated by tuberculosis. One of my patients died with a hæmorrhagic purpura and was earlier reported as having shown signs of scurvy. I have recently seen a fatal case under the care of Dr. Whittle at Addenbrooke's Hospital, in which a confluent hæmorrhagic eruption, unlike anything which I have previously seen, appeared all over the chest and abdomen together with vomiting due, as was shown at necropsy, to acute duodenal ileus from kinking of the duodenum over the preternaturally sharp edge of the root of the mesentery. Emaciation from other causes has been known to predispose to duodenal ileus and the possibility of this condition as a physical basis for vomiting in anorexia nervosa should clearly not be forgotten. Of my five male cases three recovered and engaged in full active life again ; one improved slowly but incompletely ; one died of tuberculosis of the lungs.

Treatment

Treatment consists in firm and kindly handling and insistence on an adequate food intake from the beginning. The patient should be kept in bed at first and, whenever suitable arrangements can be made, away from home. I have seen no reason to employ insulin, small doses of thyroid, or other endocrine preparations, or to allow periodic fast days as advocated by Allison and Picton Davies [1]. I have no experience of vitamin B injections. Such treatments overlook the fact that " the want of appetite " as Gull insisted, " is due to a morbid mental state " and that the treatment of starvation is feeding. Elaborate psychiatric methods are undesirable, but a simple, straightforward explanation and reassurance so framed as to convey the impression that the situation is fully comprehended and that the treatment must be accepted and will produce the desired recovery may be as important as any of the other details of treatment. The mother and daughter should be separately interviewed.

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Dr. J. H. Sheldon: Although the English literature on anorexia nervosa presents quite a tranquil surface, there is a very considerable ferment of opinion going on in American and Continental literature, and some attempt has to be made to integrate what appear at first sight to be two quite sharply contrasted points of view.

The English tradition of anorexia nervosa is entirely a development within the original framework of ideas provided by Sir William Gull, and it has for its central tenet the view that the disease is not organic, but arises from what Sir William Gull himself described as a " morbid mental state "—in other words it arises in response to some emotional or mental need, and just because I shall be devoting myself entirely to the physical aspects of the disease I am anxious at the outset to express my entire acceptance of this point of view and to say that in my judgment no account of anorexia nervosa can be even remotely adequate which fails to take cognizance of this as an essential background to the clinical features presented by the patient.

A further tenet of the English tradition is that the clinical features of the established disease are the simple result of starvation—though no one seems to have posed the question as to why starvation should produce the symptoms it actually does. In one respect, however, this is demonstrably wrong. I refer to the amenorrhœa. In between a third and half of the cases this arises at either the same time as the anorexia or even before it, and it cannot possibly then be attributed to starvation. The menses may cease suddenly as the result of mental strain or of shock in healthy women, and if proof of this be required one need only refer to the recent work of Macgregor [1] who found that among the first-year nurses at the Edinburgh Royal, no less than 29% had during the first year of their training an amenorrhœa of from one to ten months' duration. Such a functional amenorrhœa is accompanied, as one might expect, by a diminution or total absence of excretion of sex hormones in the urine. I think we are entirely justified in transferring this to anorexia nervosa, and regarding the condition there as an " amenorrhœa nervosa ". The fact that in these cases a psychological cause leads—presumably via the hypothalamus—to a suppression of hormone output from the anterior pituitary lends an initial support to the view I expressed in 1937 that the symptoms of anorexia nervosa might be explained as a sort of functional Simmonds' disease, though, as will be seen later, I no longer regard this as an adequate statement. The English tradition has also, I think, to find room for a constitutional tendency—at any rate in the cases occurring in puberty. There is evidence that a proportion of these cases were abnormal before the onset of the anorexia—usually showing evidence of a failure of growth, either bodily or sexual.

Turning to the foreign literature the first thing to note is that the original papers of Gull [2] and Laségue [3] had little influence outside their countries of origin, and in particular they remained almost entirely unknown in German-speaking countries. Indeed up to about 1930 anorexia nervosa seems to have attracted no special attention in Germany and it appears to have been regarded merely as a curiosity in the department of hysteria. Thereafter interest in the condition suddenly became active. This was due to two factors, partly to the growth of knowledge of the wide range of activity of the anterior pituitary, but mainly to the gradual popularization of the description by Simmonds [4] of the clinical effects in the human being following destruction of the anterior pituitary. As these gradually coloured the background of medical thought, so physicians suddenly woke up to the fact that there were in their midst large numbers of young women who were not only extremely wasted, but who at times actually died of their wasting. Starting *de novo*, knowing nothing of anorexia nervosa, it is not surprising that seen through such spectacles the cases were regarded as instances of organic disease. Two things happened. In the first place, large numbers of cases were described, and are still being described, in all good faith, as instances of Simmonds' disease. In actual fact there are over 80 instances of this mis-reporting and approximately half of the published cases of anorexia nervosa are indexed under other names. At the same time certain observers,

shrewder than the rest, noticed that these cases were not quite the same as those belonging to the classical type described by Simmonds, and these tended to think that they were dealing with a new disease. In actual fact the disease has been rediscovered and renamed four or five times since 1930. Falta [5] in 1928 described it as primary anorexia, and he thought that the defect of appetite was attributable to a defect of the insulin mechanism. In 1935 Korbsch [6] considered it was caused by a primary atrophy of the gastric mucous membrane. In the same year Wahlberg [7] in Scandinavia labelled it as asthenia gravis hypophyseogenea, and in 1936 Krause and Müller [8] labelled it severe anterior pituitary weakness. The most industrious of these was Kylin [9] of Sweden. In 1935 he wrote a monograph on Simmonds' disease which will always be one of the more important papers on anorexia nervosa. By 1937 he had come to realize that these cases were different from the classical form of Simmonds' disease, and so he renamed it himself. He would have liked to call it pituitary hypobasophilia, as he found a deficiency of basophil cells at post mortem, but thinking that it was probably not quite so simple he called it by the cumbrous title of " wasting of late female puberty, a disease form *sui generis* ".

The problem we are therefore presented with is this—how is it that so many observers—men like ourselves except that so far as they are concerned Sir William Gull might never have existed—how is it that they universally regard the condition as organic and with almost complete unanimity incriminate the anterior pituitary as the cause of the disease ? In some fashion we have to incorporate into the English way of looking at anorexia nervosa an adequate explanation for such a widespread error.

This is best done, I am sure, by examining the physical symptoms of anorexia nervosa in the light of what occurs in both Simmonds' disease and starvation. These three conditions have the following physical features in common : (1) loss of weight, (2) amenorrhœa, (3) lowered basal metabolism, (4) alterations in carbohydrate metabolism, (5) subnormal temperature, (6) slow pulse, (7) hypotension. So far as Simmonds' disease is concerned, I have taken into account only the cases with a pure destructive lesion of the pituitary, cases caused by infarction after labour. The facts, so far as starvation is concerned, are taken partly from the experiments of Benedict [10] and others on professional fasters, but wherever possible from the literature of famine, for this presents the closer similarity to what is found in anorexia nervosa. I shall not deal with each symptom separately, but merely state that there are no essential differences between either of the three conditions in any symptom. If one notes the widespread agreement, covering so many different fields, cardiovascular, sex, heat production, metabolism, and so on, I think one is justified in saying in the first place that the agreement is far too close to be a matter of mere coincidental similarity. Considering only starvation and Simmonds' disease—since anorexia nervosa is *sub judice*—one is forced to the conclusion that at some stage a common path is used in the production of these symptoms. If this be the case it is very important to remember that the starting place in point of time in the case of Simmonds' lies in an actual destruction of most of the anterior pituitary, while the starting place in the case of starvation lies in a lessened intake of food. This being the case it seems justifiable to advance the hypothesis that the varied changes found in starvation are not a series of haphazard peripheral effects, produced locally in this or that tissue by a mere diminution of food supply, but are a series of co-ordinated changes produced by a central mechanism adjusting the body to a lowered intake of food. Bearing in mind the past history of life on this earth, it seems inherently probable that some such mechanism would in the course of time have been evolved. It would appear, therefore, that such a mechanism—and the fact that similar mechanisms for dealing with heat and cold are situated in the hypothalamus would suggest a similar localization—acts primarily and chiefly by a general inhibition of anterior pituitary activity. The immediate recovery with normal feeding after starvation shows that the changes are

not due to an actual destruction of the pituitary cells. Such a general inhibition of anterior pituitary activity would lead to the same clinical picture as the diminution caused by actual destruction of the gland cells, and this would explain the close similarity between starvation and Simmonds' disease. Writers on anorexia nervosa speak usually of the effects of starvation as if no other explanation were required than the mere use of the word, but this is clearly insufficient, and I suggest that the similarity between the two states is as close as it is because the body adjusts itself to a lowered food intake by an immediate decrease in anterior pituitary activity—in other words by producing a functional Simmonds' disease. At the moment, therefore, it is merely a question of words whether one regards the signs of anorexia nervosa as being a functional Simmonds' disease or as being due to starvation.

There is one symptom, however, in which anorexia nervosa departs from Simmonds' disease. An increased growth of hair has never been described in any of the case-reports of Simmonds, whereas it is frequent in anorexia nervosa. The usual finding is a growth of downy hair on the trunk and limbs, while on the face the hair is masculine in tendency, with downy hair on the moustache area, and coarser hairs on the beard region. I have had great difficulty in finding what happens in famine, but I recently came across the following quotation from a lay observer describing what he saw in what I take to have been the great Irish potato famine of 1845 [11]. The Rev. Canon Bourke, of Claremorris (quoted by Curran), said, " I saw hundreds of children, from the ages of 2 to 12, with hair on their skinny arms and cheeks fully one inch long, a false growth caused by decay and hunger. A lad of 12, whose cheeks were wan as those of a corpse, invested with the cerements of the grave, and who presented all the usual features of chronic starvation, exhibited this peculiarity in a striking manner. The lad's arms were covered throughout with downy hair ". That exactly parallels what is found in anorexia nervosa, and in this respect, therefore, the disease departs from Simmonds' and follows starvation. This increased growth of hair supports my suggestion that the body adapts itself to starvation by a series of co-ordinated and not haphazard local changes—for this growth of hair has an obvious teleological significance—to assist in preserving the body heat. It is also worth noting that if one attributes it to some increased activity of the suprarenal cortex, then the intersexual features of the hair growth, which are also found in starvation, may be regarded as an unnecessary but inevitable by-product of this activity, and it is worth noting that alone among the endocrine organs, the suprarenal gland enlarges during starvation, and was found by T. R. Elliott [12] as long ago as 1914 to be remarkably well preserved in anorexia nervosa. The physical changes in anorexia nervosa are therefore identical with those of starvation, and if one regards the latter as the result of a co-ordinated mechanism which in many respects involves a great diminution of anterior pituitary activity, one can readily understand why anorexia nervosa is so universally regarded abroad as an organic endocrine disorder. Since such an explanation in no way disagrees with the view that the origin of the starvation is psychological, it fits in readily enough with the English tradition, and it is difficult to see any other way in which the two points of view can be brought together.

I would say, therefore, that in response to an original cause on the mental plane, there is a loss of appetite and in some cases a simultaneous cessation of menstruation due to a direct nervous inhibition of sex hormone activity in the anterior pituitary. The lowering of food intake sets in motion a mechanism which acts mainly by a reduction of anterior pituitary activity, and therefore mimics the clinical tableau of organic disease of the pituitary.

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Dr. A. W. Spence: Anorexia nervosa presents various problems of interest to the endocrinologist. I propose to deal mainly with the endocrine aspect of the condition, and to present for your criticism a few thoughts on the mechanism whereby the disturbances of the endocrine system are produced.

At the outset I must stress that I do not consider anorexia nervosa to be primarily a disease of the endocrine system. I agree with the previous speakers that the initial disturbance is psychological, the manifestations of endocrine dysfunction being purely secondary. These may be so prominent that the condition may be, and often is, mistaken for Simmonds' disease. In fact, when discussing a patient with anorexia nervosa with a physician from Germany, I was informed that in that country the term anorexia nervosa is not recognized, and that the patient in question would be considered to be suffering from Simmonds' disease. The syndrome described by Simmonds, however, is in my opinion a rare condition, the diagnosis of which is frequently uncertain until autopsy, but milder forms, described by von Bergmann (1934) as pituitary emaciation, are more common. In passing, I would suggest that pituitary emaciation is a better term for these milder cases than Simmonds' disease, as they do not conform to the picture originally described by Simmonds. The symptom-complex of anorexia nervosa and pituitary emaciation is often indistinguishable, but in looking through the literature on the subject, I have found a number of cases labelled pituitary emaciation which, in my opinion, would have been more correctly diagnosed as anorexia nervosa. The differentiation between the two conditions rests mainly on the discovery of an initial psychological factor, which is responsible for the loss of appetite in anorexia nervosa.

The mechanism whereby a psychological disturbance causes loss of appetite is not clear. Hunger, however, depends on the muscular contractions of the empty stomach, but after a few days of fasting, hunger contractions cease (Cannon and Washburn, 1912). Ross (1938) has drawn attention to the fact that hunger is related to a fall in the blood-sugar level (Bulatao and Carlson, 1924). He has pointed out that partial starvation at once leads to impaired glucose tolerance, and that if hunger contractions are dependent on a low level of the blood-sugar they will cease at the higher fasting level which is present in impaired tolerance, and consequently hunger will fail. This accounts for the emaciation which sometimes affects obese subjects who have undergone slimming.

The occasional appearance of amenorrhœa before anorexia has been used by some writers as one argument in favour of anorexia nervosa being primarily an endocrine disorder. As menstruation is dependent on the delicate balance of ovarian hormones, the secretion of which is controlled by the anterior pituitary, amenorrhœa, in the absence of a general debilitating condition such as anæmia, is necessarily of endocrine origin, but in anorexia nervosa not necessarily of *primary* endocrine origin, as it is for instance in a patient with a chromophobe adenoma of the pituitary. There is anatomical evidence that nerve-fibres pass from centres in the hypothalamus to the pituitary, and it is suggested that the secretion of pituitary hormones is a response to stimuli from these centres (Beattie, Brow and Long, 1930). Ovulation and pseudo-pregnancy have been induced in animals by electrical stimulation through the head

(Harris, 1936 ; Marshall and Verney, 1936), and Theobald (1936) has produced clinical evidence to show that the regularity of the menstrual cycle probably depends on the passage of nervous impulses from a menstruation centre in the hypothalamus to the anterior pituitary. It is well known that even the slightest psychological disturbance may cause amenorrhœa. It is conceivable that the outflow of impulses from the hypothalamic centres to the pituitary are inhibited by a disturbance of the higher centres. One calls to mind that a similar sequence of events may be sometimes responsible for the production of diabetes insipidus. There is thus no reason why amenorrhœa should not precede anorexia as a symptom of disturbance of the higher centres.

After the anorexia has become established, I feel that the endocrine features can be explained in terms of vitamin deficiency. A likely cause of the amenorrhœa, in addition to the psychological disturbance, may be the deficient intake of vitamin E. Rowlands and Singer (1936) have found that the pituitary gland of rats fed on a vitamin-E-deficient diet contains a decreased amount of the gonadotrophic hormone which causes luteinization of the ovarian follicles. Barrie (1937) has drawn attention to the similarity of the effects of hypophysectomy to those produced by vitamin-E deficiency, and suggested that the two phenomena may be related. She found that in rats fed on a vitamin-E-deficient diet the anterior pituitary contained a large number of agranular cells ; the eosinophil cells were small and degenerate, and the thyroid was hypoplastic. Ovulation and œstrous cycles were apparently normal, but in one animal whose mother was partly E deficient the ovaries showed no normal follicles. Barrie concluded that vitamin E is necessary for the normal function of the anterior pituitary, and that in E-deficient rats the secretion of gonadotrophic and thyrotrophic hormones is impaired. Admittedly, so far as animal experiments indicate, and these have been conducted mainly on the rat, vitamin E is directly concerned with only one phase of the female reproductive process, namely the blood supply and nutrition of the embryo, but it is well known that the reaction of different species, not only to pituitary hormones, but also to vitamin deficiency, varies considerably. I feel, therefore, that in view of the marked changes demonstrable in the anterior pituitary of vitamin-E-deficient rats, one should seriously consider whether an additional cause of the amenorrhœa in anorexia nervosa may possibly be the deficient intake of vitamin E, resulting in impairment of anterior pituitary function, deficient secretion of gonadotrophic hormone, and consequently defective formation of the corpus luteum and diminished secretion of progesterone. The estimation of the output of pregnanediol in the urine in this condition would be of considerable interest.

In addition, deficiency of vitamin A has been shown to prevent the characteristic action of gonadotrophic hormone (Aberle, 1933), so that deficiency of vitamin A may also play a part in anorexia nervosa by preventing the action of whatever gonadotrophic hormone is secreted.

A prominent feature in anorexia nervosa is the low basal metabolic rate, a usual finding in undernutrition. Lusk (1928), who observed this in professional starvers, suggested that it was an innate protective mechanism, the nature of which one could only dimly surmise. This view was supported by Berkman (1930), writing on anorexia nervosa, but as Dr. Sheldon (1937) has pointed out, it does not take into account the mental and bodily activity which is so common in these patients. Reference has already been made to the thyroid hypoplasia and changes in the anterior pituitary in vitamin-E-deficient rats. Similar thyroid changes were found in vitamin-E-deficient rats by Singer (1936), who also concluded that the proper functioning of the pituitary undoubtedly depends in some degree on the presence of vitamin E in the tissues. I put forward the suggestion that a deficiency of vitamin E, acting through the anterior pituitary and diminishing the output of thyrotrophic hormone, may be responsible for the low basal metabolism in anorexia nervosa.

So far we have considered only the effect of vitamin deficiency on the anterior pituitary, without reference to its effect on the receptor glands, such as the thyroid and ovaries, which the anterior pituitary stimulates. Extracts of anterior pituitary or of pregnancy urine or progesterone do not prevent the reproductive failure in rats fed on a vitamin-E-deficient diet (Mattill, 1938), so that it appears that in the absence of vitamin E in the tissues these hormones are unable to exert their usual action. With regard to the thyroid, a deficiency of vitamins has a definite effect on its structure and function. Some years ago I showed that in the rat vitamin-A deficiency produces considerable keratinization of the thyroid epithelium, with a fall in basal metabolism in some of the animals (Spence, 1932). In vitamin-B deficiency the specific dynamic action of protein is not observed, probably owing to diminution in thyroid secretion (Arvay and Verzár, 1928). Singer has observed that in vitamin-E-deficient rats the thyroid response to even large doses of anterior pituitary extract is surprisingly small. This has been my experience in a patient with anorexia nervosa. The administration of thyrotrophic extract of the anterior pituitary to normal man results in a prompt rise of the basal metabolic rate within twenty-four to forty-eight hours, but in the patient with anorexia nervosa little response was obtained with 2 c.c. of ambinon (400 Heyl-Laqueur units) a day for eight days.

The response of an organ to a hormone depends not only on the activity and dose of the preparation, but also on the sensitivity of the organ to the stimulus. Thus, before a certain age the ovarian follicles are incapable of responding to injections of the follicle-stimulating hormone (Smith, Engle and Tyndale, 1934). It is suggested that the tissues of the patient in question were deficient in some substance (? vitamin A and/or vitamin E), an adequate amount of which is necessary to maintain the responsive capacity of the receptor organs, e.g. the thyroid. This may perhaps be the reason why I have found hormone treatment disappointing. The administration of thyrotrophic extract, the follicle-stimulating extract of pregnant mare's serum and œstradiol benzoate, has failed to bring about the slightest improvement. It did not occur to me at the time, about eighteen months ago, to determine the effect of thyrotrophic hormone after giving full doses of vitamin E, and since then the opportunity has not recurred.

If it is true that these patients are suffering from vitamin deficiency, the keratinizing action of vitamin-A deficiency on the thyroid epithelium and the impairment by vitamin-E deficiency of the capacity of the thyroid to respond to thyrotrophic hormone are further reasons why the basal metabolism is low in anorexia nervosa. On the other hand, it is remarkable that these patients never demonstrate the more severe nutritional disorders—scurvy, beri-beri, nutritional œdema. It is possible that the endocrine system is more sensitive to vitamin deficiency.

I do not propose to say much about treatment. As the disorder is primarily due to inability to take food, initially because of a mental upset, and later perhaps because of impaired sugar tolerance in addition, treatment should be directed to improving the mental state and encouraging the patient to eat. The diet should not be bulky, and should consist largely of carbohydrate to bring the fasting blood-sugar to a lower level, in the hope that thereby hunger contractions will be initiated. Some of my remarks on the mechanism of anorexia nervosa have been somewhat hypothetical, as I have not yet had the opportunity of putting them to a practical test, but for the reasons I have suggested it would be well worth trying the effect on the endocrine disturbances of full doses of vitamins, especially of vitamin E.

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Sir Arthur Hurst: In anorexia nervosa the loss of appetite itself is generally due primarily to some psychogenic cause. Sometimes, however, it is secondary to a voluntary restriction in the intake of food, again due to some psychogenic cause, but in this case the anorexia results from the physiological fact that the appetite varies with the intake of food, the anorexia being the natural sequel of an insufficient diet. Whether the anorexia is primary or secondary to a diminished intake of food it is likely to continue indefinitely unless the patient makes a voluntary effort to overcome it, as the longer the abstention from food remains the more pronounced is the resulting anorexia.

It is clear, therefore, that the logical treatment is to reverse the process and to overcome the anorexia by persuading the patient to eat. It is quite unnecessary at this stage to tackle the primary psychological troubles, and such accessory treatments as the use of pituitary or ovarian extracts, insulin, vitamins, or special diets, are also quite unnecessary. Treatment is extremely difficult at the patient's home and hardly less difficult in the general ward of a hospital, but comparatively easy in a nursing home. We have had the opportunity of treating about 50 cases at New Lodge Clinic since 1921 and without exception they have done well.

The patient is made to realize that the physician fully understands her difficulties. She is told that in spite of her nausea, loathing of food and discomfort on eating she must eat, as it is only by eating that she can re-educate her appetite. It was lost by fasting; it will be restored by eating. The process will be uncomfortable, but it can and must be carried through. After one long conversation a full meal is given, and the patient is not left until the whole of it has been consumed. There must be no time limit for this first meal; resistance is often extreme, but it can always be overcome with patience and good temper. After success with the first meal progress is generally uninterrupted. Resistance still occurs in many cases, but it becomes rapidly and progressively less. In a severe case it may be necessary for the physician to be present at one meal a day for the first week or fortnight, but the management of the remaining meals may be left to an experienced nurse.

When the appetite is returning and the patient is eating full meals without difficulty, the psychological problems which led to the anorexia may be discussed, but this is not always necessary, as in many instances they have been forgotten in the severity of the illness that followed or they have solved themselves by the time the patient has come under treatment. A few straightforward conversations are sufficient to reveal and straighten out most mental tangles. No form of deep analysis is ever required.

The ultimate prognosis is excellent. I have never seen a case in which the cure of the anorexia was followed by the substitution of some other hysterical symptoms. Several of our cases date from ten or fifteen years ago, and so far as I know there has been no recurrence. The worst case I have ever seen, a boy aged 19, who was almost moribund on admission and so weak that he could not speak above a whisper or raise his head or arms, made a perfect physical and mental recovery, and now, seventeen

years later, he is a successful business man with a family of three children. He was the only case in which a full diet could not be given, as he was not only too weak to feed himself but was also firmly determined to take no food of any kind if he could help it. A tube was passed through his nose into his stomach and milk from a concealed retainer was run in by the drip method continuously day and night for five days, by which time he had recovered sufficient strength to feed himself and sufficient sense to agree that the taking of food was not a sin and that life was worth living.

Dr. S. W. Patterson: In a series of 273 patients observed at Ruthin Castle in whom the main or a prominent symptom was loss of or grossly lessened appetite, it was found that organic disease of the stomach (ulcer, carcinoma, gastritis, or the after-stages gastro-enterostomy) which may interfere seriously with the appetite, accounted for one-quarter of the cases. In one-eighth of the patients reviewed, appetite was much diminished reflexly from disease elsewhere in the alimentary tract originating in the lower bowel, carcinoma of colon or rectum even in the early stages before asthenia or exhaustion from pain occurred, colitis especially ulcerative, or affections of the gall-bladder, cholecystitis, gall-stones.

The largest group, just under one-half, consisted of toxic, infective, and general states. Of these one-third follow the breakdown of cardiorenal cases, congestive failure or uræmia; one-half are due to anæmia, arthritis, infections of urinary tract, phthisis, and other infections; a few fall into a degenerative group, with the waning powers of senescence. In an endocrine group of 10 cases, seven were related to the thyroid; two were cases of myxœdema, one had a goitre pressing on the trachea, and four were cases of Graves' disease. All did well on treatment, the first two with thyroid extract, the others with the surgical removal of the excess of gland substance. Two were related to cessation of ovarian function rather than to neurosis. One was a diabetic, in whom the distaste and monotony of strict diabetic diet produced starvation and anorexia. This may be compared with a patient who began dieting himself for intolerable migraine, becoming vegetarian, reducing his weight, and ending with distaste for food and anorexia.

Nervous factors accounted for one-fourth of the cases: psychoses, anxiety, and neurasthenic psychoneurosis, and the type (in nine patients of the series) recognized as anorexia nervosa.

Local—		
Peptic ulcer, atrophic gastritis, gastro-enterostomy	26	
Alcoholic gastritis	21	
Carcinoma	16	
	—	63
Reflex—		
Colon or rectum (colitis, carcinoma)	19	
Gall-bladder, cholecystitis, gall-stones	14	
	—	33
Toxic—		
Cardiorenal	37	
Chest (phthisis, carcinoma)	10	
Anæmia (secondary, Addisonian, Hodgkin's)	16	
Carcinomatosis	4	
Arthritis	9	
Pyelitis	7	
Other infections (malaria, shingles, antrum)	9	
Endocrine (menopause, diabetes, thyroid)	10	
Degenerative	7	
	—	109
Nervous—		
Psychotic	14	
Strain	28	
Anxiety	17	
Anorexia nervosa	9	68
	—	—
		273

The psychotics are in a group by themselves, but I think it is justifiable to divide the other cases of functional anorexia into those with anxiety neurosis, those with nervous exhaustion or strain, and anorexia nervosa in the restricted sense. Usually there is a history of anxiety, strain, or disappointment and emotional conflict.

Very few of these cases are in our experience endocrine in origin. As in the War, the breaking strain of individuals varies greatly, and after a breakdown it often takes a long time to pick up. In most cases institutional treatment is advisable; the nursing care and the feeling that all worries are shouldered by someone else, at least for the time being, are a great help. The essential form of treatment is by improving the nutrition; this may be done both by reducing the expenditure of energy—these patients are usually ceaselessly active and should be rested in bed with mild sedatives at first—and by increasing the diet, giving small frequent meals of concentrated foods.

In all three groups the psychological aspect must be taken into account. In the group brought about by strain, the rest, relief from work, may be enough, but rest has to be promoted by sympathy and sedatives; in the group with anxiety, much reassurance is needed; in the true anorexia nervosa, during the stage which is almost mental, firm but kindly discipline is required.

Dr. Henry Yellowlees associated himself with the remarks of the previous speaker, and pointed out that they gave some little indication of the infinitely complex and important state of affairs underlying what had been rather glibly summarized as "the mother-daughter relationship". He was surprised that, after the earnest emphasis laid by all three openers upon the essential "psychological factor" in causation, the references to the treatment of this factor had consisted in little more than a warning to avoid "elaborate psychotherapy" and an exhortation to "speak kindly but firmly to the patient". He fancied he had heard these words before.

He said that, in the majority of cases, anorexia nervosa was a symptom of hysteria—using that word in its proper sense—and he contrasted it with the refusal of food that might occur in practically every psychosis, and also with the similar but, as he thought, quite distinguishable syndrome of "pituitary cachexia" or Simmonds' disease.

He pointed out that no reference had been made to the widely differing effects of starvation or limited intake of food in different circumstances, e.g. in famine, in anorexia nervosa, and for therapeutic purposes.

Dr. F. Parkes Weber said that in severe cases of anorexia nervosa it seemed to him almost criminal to waste time in anything like psycho-analytical investigations (however interesting they might be) at the commencement of treatment.