ACHLORHYDRIA IN THE PSYCHOSES: WITH SPECIAL REFERENCE TO COINCIDENT ANÆMIA.

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THE incidence of achlorhydria and its association with certain forms of anæmia has recently been the subject of much interest, largely owing to the work of Witts (1, 2) on idiopathic hypochromic anæmia, and of Hurst (3) on pernicious anæmia.

An opportunity of investigating a number of psychotic patients having presented itself, it seemed worth while to correlate fractional gastric analyses and blood-counts in a series of cases. The purpose of this study was threefold: firstly, to determine the frequency of achlorhydria in psychotic patients as compared with normal individuals; secondly, to ascertain whether achlorhydria was peculiar to, or predominated in, any particular psychosis; and, lastly, to inquire into the occurrence of forms of anæmia in achlorhydric, psychotic subjects.

Publication has been made possible through the kindness of Dr. D. F. Rambaut, Medical Superintendent of St. Andrew's Hospital, who has also permitted me to include in my figures (for statistical purposes only) some analyses and blood-counts carried out in the laboratory of Wantage House during the term of office of my predecessor, Dr. W. M. Ford Robertson.

Grateful acknowledgments are due to my colleagues, Dr. N. R. Phillips, D. J. O'Connell and J. McLeman, for allowing me to abstract their clinical notes of illustrative cases.

Chemical examination of the fractional test-meals was carried out with the assistance of Mr. C. Webb, for whose help I am greatly obliged.

The fractional test-meals were performed by the Rehfuss method, a Ryle's tube being passed and the resting juice withdrawn before the meal, consisting of a pint of oatmeal gruel, was given. About 10 c.c. of the gastric contents were subsequently aspirated every quarter of an hour for two hours, or for as long as the patient would allow the tube to remain *in situ* up to two hours.

INCIDENCE OF ACHLORHYDRIA IN THE INSANE.

No very large series of observations on fractional gastric analyses in psychotic patients is available for reference. The reason is fairly obvious. Co-operation of the patient is essential for the examination, and in many cases

it is necessary to postpone the test until the patient is willing, or is able, to co-operate.

Gamble (4) examined 149 patients by the fractional meal method, of whom 20·8% had complete achlorhydria, and 7·3% had less than ten degrees of free acidity at any time during withdrawal of the meal. No one psychosis was found to be particularly associated with achlorhydria. All the chief forms of insanity were included amongst the cases investigated. Northcote (5), in a small series of 23 cases, found that 3, i.e., 13%, were achlorhydric. She also failed to establish any relationship between achlorhydria and particular psychoses.

Before considering the results obtained in the series of 300 fractional test-meals carried out at Wantage House, reference must be made to the question of the incidence of achlorhydria in healthy subjects, and especially to the influence of age upon the secretion of hydrochloric acid.

Since Bennett and Ryle (6) found that 4 out of 100 healthy medical students exhibited achlorhydria several series of cases have been published, some of which clearly indicate the effect of increasing age upon the acidity of the gastric contents. The largest series yet reported is that of Connor (7), from the Mayo Clinic. In this series, 15·2% of 5,000 patients were found to have achlorhydria, but all of these were under suspicion of having some disease of the gastro-intestinal tract. Hartfall (8) analysed the results of over 2,000 test-meals performed at the New Lodge Clinic, grouping each decade separately. Out of a total of 2,248 cases, 336 (13·7%) had achlorhydria. One of the most interesting facts which emerged from Hartfall's investigation was the rate at which the secretion of free acid declined with advancing age. In the second decade Hartfall found that only 3·8% of his patients had achlorhydria, which figure is practically the same as Bennett and Ryle gave for students of approximately the same age. But in the age-period 30 to 39 years the figure rose to 9·2%; in the fifth decade it was 14·3%, whilst between 60 and 69 no less than 20% of the patients were achlorhydric. A similar observation was made by Davies and James (9), who performed a series of test-meals in 100 healthy persons over the age of 60 years. Their findings put the percentage of achlorhydria in the elderly at an even higher figure, 32% for people over the age of 60. This observation is of particular interest, as the patients investigated by Hartfall were at least suspected of having some disorder, though not necessarily of the gastro-intestinal tract, whilst those of Davies and James were considered quite healthy. In this last series pepsin was not entirely absent in any case of achlorhydria, there being therefore no cases of true achylia gastrica in the series.

In any attempt to assess the relative occurrence of achlorhydria in different groups of patients, the normal variation in secretion of free acid at various ages must obviously be taken into consideration. The average age of patients in mental hospitals (excluding institutions for mental defectives) is relatively

high. (The average age on admission to St. Andrew's Hospital for the last ten years was 46·8 years.) Therefore the incidence of achlorhydria in a large unselected group of patients at this hospital would, according to Hartfall's figures, be approximately 15%.

Of the 300 last cases investigated at Wantage House by the fractional meal method, actually only 32 (10·6%) had complete achlorhydria, although another 13 (4·3%) had less than six degrees of free acidity at any time during withdrawal of the meal. Although the percentage of cases showing a very small amount of free acid has been mentioned as a matter of interest, cases of complete achlorhydria only will be discussed, as it is obviously unjustifiable to include as achlorhydrics cases showing even a trace of free acid.

In this series, therefore, 10·6% only showed complete achlorhydria—a percentage lower than would have been expected for the age of the patients.

Achlorhydria in Relation to Various Psychoses.

In trying to determine whether achlorhydria predominated in any particular psychosis, the age-factor again came into play. On first consideration of the figures it seemed as though in those patients who were depressed, either in one phase of the manic-depressive psychosis, or as a feature of involutional melancholia, achlorhydria was twice as common as in any other psychosis. Actually 12 of the 32 cases of achlorhydria (37·5%) occurred in depressed subjects. But on examining the figures more closely the fallacy became obvious; the average age of cases of depression was far higher than the average age of the total number of achlorhydrics. The average age of the depressed cases was 64·8 years; that of the total number of achlorhydrics was 47·5 years. As at least 20% of healthy individuals over the age of 60 years show achlorhydria, it is not surprising that this should occur more commonly in states of depression in which the average age is over 60 years than in psychoses which occur at an earlier age. No significance can therefore be attached to the apparently high incidence of achlorhydria in melancholia. The other psychoses which were represented amongst the cases of achlorhydria were paraphrenia, schizophrenia, mania, and the anxiety state.

The Occurrence of Anæmia in Association with Achlorhydria in the Psychoses.

The two chief forms of anæmia which are particularly associated with achlorhydria are Addisonian (or pernicious) anæmia on the one hand, and the idiopathic, hypochromic anæmia of Witts on the other. As no example of the latter condition occurred in the series under investigation, it must remain undiscussed, with the comment that special attention was paid to the blood-count in the case of any patient, achlorhydric or otherwise, who seemed at

all likely to be anæmic. All cases in which a test-meal was carried out had at least one, and many had several blood-counts done. It is therefore improbable that a case of hypochromic anæmia would have been overlooked.

Numerous investigators have focused their attention on the frequency with which anæmia occurs in achlorhydric subjects. Faber (10) found that out of 207 cases of achlorhydria there were 22 cases (10·6%) of pernicious anæmia and 52 (25%) of anæmia with a low colour index. More recently Faber and Gram (11) analysed a series of 90 cases of achylia, and found that, excluding examples of pernicious anæmia, the percentage of cases of anæmia was as high as 41. In Borgbjaerg and Lottrup's series (12), there was an anæmia in 50% of the cases, though in the majority this was of slight degree and of a secondary, hypochromic type. In 22%, however, the colour index was above unity and megalocytosis occurred in 15%. Witts (1), in writing on idiopathic hypochromic anæmia in 1930, stated that in 100 patients with achlorhydria uncomplicated by neoplasm or other serious disease, one might expect to find 10 with Addisonian anæmia and 20 with a secondary anæmia. Hartfall (8) reported 53 cases (15·7%) of pernicious anæmia and 32 cases (9·5%) of secondary anæmia in his series of 336 cases of achlorhydria. Davies and James (9), in their study of achlorhydria in the elderly, found that in 7 cases out of 14 with " true " achlorhydria (i.e., giving no secretion of free acid after injection of histamine), there was some degree of anæmia, whilst in a group of 13 cases in which hydrochloric acid was secreted after histamine injection, only one had a red cell-count below four million. Of those cases with a normal acid secretion none had a red cell-count below 4·3 millions. Davies and James also determined that anæmia was more common in cases showing a diminished peptic activity than in those with a good secretion of pepsin. Their work will be referred to again.

In the St. Andrew's Hospital series, 6 cases of anæmia were discovered amongst the 32 cases of achlorhydria, i.e., 18·7%. All of these were hyperchromic in type. Four were obvious cases of pernicious anæmia—one being of special interest—of which two will be discussed in this paper. The other two belonged to a group to which little attention has been drawn, namely, a hyperchromic anæmia which occurs in the elderly, usually, but not always, associated with achlorhydria, whilst peptic activity remains good. Although this anæmia superficially resembles pernicious anæmia as regards the blood-picture, it is distinct from, and unrelated to, that condition. Lasch and Triger (13), who analysed many blood-counts in patients over the age of 60 years, found this " hyperchromia of old age " in 13 patients out of 150. They pointed out that the resemblance to pernicious anæmia depends on a colour index above unity, with poikilocytosis and anisocytosis of the red cells in a patient who probably shows achlorhydria. (This was present, however, in only 6 out of the 13 cases observed by Lasch and Triger.) It differs from pernicious anæmia, as regards the blood-picture, in that the changes in the red cells are

never as severe as in the more serious anæmia ; normoblasts and megaloblasts are absent ; the mean diameter of the red cells is not increased ; the Van den Bergh reaction is usually negative, and achlorhydria is not invariably present. Clinically, although the signs of general weakness are out of all proportion to the age and there may be gastro-intestinal disturbances, there is never any evidence of an affection of the nervous system. Although pernicious anæmia itself is not uncommon in the senium, the benign type of blood-picture which Lasch and Triger described, and of which two examples are recorded below, would seem to be more common. Davies and James (9) did not give the details of the blood-pictures in their series of elderly achlorhydrics ; they merely mentioned that some degree of anæmia was present in eight of their cases. Presumably this was a secondary, hypochromic anæmia.

CASE 1.—Mr. O—, æt. 72, was admitted to Wantage House on February 28, 1933. He was then greatly depressed over a supposed financial loss, somewhat restless, and expressed the delusion that his house had been burnt down. The clinical diagnosis of his mental state was " senile melancholia ". Nothing abnormal was found on physical examination, a careful investigation of the nervous system being completely negative, though it was noticed that he was rather feeble, even for his age.

A blood-count on March 4 gave the following result : Red blood-cells 4,144,000 per c.mm., hæmoglobin 99·4%, colour index 1·2, white blood-cells 4,000 per c.mm., polymorphonuclears 65%, large lymphocytes 23·5%, small lymphocytes 8·5%, monocytes 3%. A test-meal showed complete achlorhydria, with, however, full peptic activity. The indirect Van den Bergh test was positive.

Another blood-count on March 13 showed a definite hyperchromic anæmia : Red blood-cells 3,376,000 per c.mm., hæmoglobin 77·5%, colour index 1·17, white blood-cells 13,900 per c.mm., polymorphonuclears 54%, large lymphocytes 33%, small lymphocytes 7·5%, monocytes 4%, eosinophils 0·5%, basophils 0·5%. Marked poikilocytosis and anisocytosis of the red cells. No nucleated red cells seen. Reticulocytes 0·6%.

The patient was given half a pound of fresh liver daily from March 23 onwards. (It was much easier to persuade him to eat this than to take liver extracts by mouth.)

Blood-count on March 27 : Red blood-cells 3,288,000 per c.mm., hæmoglobin 92·3%, colour index 1·4, white blood-cells 6,100 per c.mm., polymorphonuclears 57%, large lymphocytes 36%, small lymphocytes 5%, monocytes 2%. Marked anisocytosis, with megalocytes predominating. Reticulocytes 0·97%.

On April 12, his physical condition being somewhat less feeble, and being mentally more cheerful, the patient was transferred to a villa, from which he was discharged on October 8, 1933. During this time liver treatment was continued, but, owing to firm opposition from the patient, it was not possible to do further blood-counts.

On readmission on June 21, 1934, he was unduly depressed and apprehensive. He lacked initiative, and had delusions of being followed. When in this phase of his illness he tolerated investigations which he would not permit when less depressed.

A blood-count on June 25 showed a remarkable improvement in the blood-picture : Red blood-cells 5,184,000 per c.mm., hæmoglobin 95·8%, colour index 0·94, white blood-cells 10,100 per c.mm., polymorphonuclears 60%, large lymphocytes 21·5%, small lymphocytes 12%, monocytes 5%, eosinophils 1·5%. Slight anisocytosis only of the red cells. A fractional test-meal showed that achlorhydria persisted but peptic activity was still good.

As soon as the investigations were completed, the patient was transferred to a

villa, where he gradually emerged from his depression, grew cheerful and garrulous, and has continued to reside quite contentedly up to the time of writing.

CASE 2.—Miss G—, æt. 67, was admitted to St. Andrew's Hospital on November 12, 1932, as a certified patient. Her mental state was one of depression and restless agitation. From time to time she gave expression to numerous delusions concerning her bodily condition. Progressive physical weakness was accompanied by mental deterioration. On admission no abnormal findings were noted on physical examination, but in May, 1933, routine examination revealed a tender mass in the right hypochondrium and tenderness over the epigastric region.

The result of a blood-count on May 31 was as follows: Red blood-cells 3,560,000 per c.mm., hæmoglobin 81%, colour index 1·1, white blood-cells 6,700 per c.mm., polymorphonuclears 37·5%, large lymphocytes 37·5%, small lymphocytes 18·5%, monocytes 6%, basophils 0·5%. Slight anisocytosis and poikilocytosis of the red cells. A fractional test-meal revealed complete achlorhydria, but good peptic activity at the end of an hour. An X-ray taken about this time showed a filling defect in the stomach, which lent colour to the tentative diagnosis of carcinoma ventriculi, in spite of the high colour index of the blood-count. Owing to the collapsed veins it was impossible to obtain blood for the Van den Bergh test.

Contrary to expectations the patient improved slightly in physical health for about a year, and her appetite, which had been poor, became better, though capricious. The tenderness in the upper abdomen persisted, and it was difficult on this account to palpate the mass previously felt.

By September, 1934, weakness was again pronounced and several slight seizures occurred, in which dyspnœa, cyanosis and vomiting were observed.

A blood-count on September 24 gave the following result: Red blood-cells 4,656,000 per c.mm., hæmoglobin 92·1%, colour index 1·0, white blood-cells 4,600 per c.mm., polymorphonuclears 61·5%, large lymphocytes 3·5%, small lymphocytes 33·0, monocytes 1·5%, basophils 0·5%. Slight anisocytosis of red cells.

No remarkable change occurred until about a week before death, when the patient sank into a semi-coma. Death took place on November 18, 1934.

Post-mortem findings.—No evidence was present of malignant disease of the stomach or other viscera. The mass felt in the right hypochondrium during life proved to be a cyst of the liver, about the size of a tennis ball, lying on the under-surface of that organ. Other, smaller, cysts were scattered over the surface. The fluid in the cysts was highly albuminous, contained only a trace of bile-pigments, few blood-corpuscles, but there was no evidence of the presence of a parasite. No other organ contained cysts. The liver cysts were probably of congenital origin. The heart was small (weight 8 oz.), and the myocardium was pale and flabby, but showed no fatty changes. The brain was greatly atrophied, particularly over the fronto-parietal region of the cortex. There were no other changes of note in the organs.

Microscopical examination.—The liver showed a very small amount of iron-containing pigment in the Kupffer-cells but none in the polygonal cells, and none was seen in the kidneys or spleen. No fatty changes were present in the liver. The fibres of the heart muscle were small and poorly striated, but they showed no fatty or fibrous degeneration. Examination of the cortex of the brain revealed much shrinkage of the grey matter in the frontal region, with loss of nerve-cells, especially in the deeper layers. No senile plaques and no fibrillary changes in the nerve-cells were to be seen.

These two cases illustrate a form of hyperchromic anæmia with a high colour index, which occurs in the senium. A possible diagnosis of pernicious anæmia in Case 1 was ruled out by the normal peptic activity, which showed that although there was achlorhydria, true achylia gastrica was not present. A few, very few, cases of pernicious anæmia have been recorded in which

achylia gastrica has been absent, but these cases are so rare that for practical purposes it may safely be said that the presence of normal gastric ferments negatives a diagnosis of pernicious anæmia. The absence of clinical signs, such as glossitis, in this case was also against this diagnosis. Response to liver treatment was good, and although mentally the patient did not improve greatly, his physical condition progressed favourably. The psychosis in this case was associated with the senility and not with the anæmia.

In Case 2 liver treatment was not undertaken, as the clinical and X-ray findings were overwhelmingly in favour of a diagnosis of carcinoma of the stomach. The absence of any post-mortem or microscopical evidence of carcinoma, pernicious anæmia or subacute combined degeneration of the cord, appeared to justify inclusion of this case in the group of senile hyperchromic anæmias. It is unfortunate that no bone was removed at autopsy for study of the bone-marrow. The psychosis in this case also was unrelated to the coincident anæmia.

Of the four cases of pernicious anæmia encountered in this series of achlorhydrics (12·5%), two have already been recorded in this journal by Phillips (14). Of the remaining two, one was of particular interest, as the anæmia and the psychosis associated therewith followed a sub-total gastrectomy performed ten years previously.

The occurrence of any form of anæmia after gastrectomy is certainly rare. Vaughan (15) was able to collect only 122 cases in the literature, whilst Lake (16) found no cases of anæmia in a follow-up of 56 cases of partial gastrectomy. The rarity with which gastrectomy is followed by pernicious anæmia may be gauged from the fact that Rowlands and Simpson (17) were able to trace only 15 such cases in 1932 when recording 2 of their own. Since then Ungley (18), in reporting one which occurred in the very short space of time of five months after a total gastrectomy, mentioned four more, and Davidson (19) had referred to two others under his care. Altogether there would seem to be only 24 cases on record of post-operative pernicious anæmia.

The type of operation performed has a considerable bearing on the subsequent development of anæmia. Morley and Roberts (20) found that a severe anæmia was more likely to follow a Polya than a Schoemaker gastrectomy. The Polya operation apparently abolishes gastric secretion entirely, whilst after the Schoemaker procedure secretory capacity may be re-established. In the case to be recorded a Polya operation was performed.

One of the most remarkable features of pernicious anæmia following gastrectomy (apart from the question as to what determines which patients who undergo gastrectomy will develop pernicious anæmia) is the time which may elapse between the operation and the onset of the anæmia. One of Rowland and Simpson's patients remained free from symptoms after a partial gastrectomy for fifteen years before developing pernicious anæmia with subacute combined degeneration of the cord; and in their other case nine years

elapsed between the operation and recognition of the anæmia. An interval of more than five years between operation and symptoms of anæmia has several times been recorded, as in the cases of Berger (21), six years; Hochrein (22), two cases, eight and six years; Dennig (23), two cases, nine and eight years; Morawitz (24), two cases, eight and six years; and Breitenbach (25), six years. These long latent periods are all the more remarkable because, except in the cases of Morawitz, Berger, and Rowlands and Simpson, a complete gastrectomy was performed in every case.

In the case to be recorded, about five-sixths of the stomach had been removed ten years before the onset of symptoms of general weakness gave rise to the suspicion that an anæmia was present. The association of mental disturbances with pernicious anæmia following gastrectomy has not, as far as could be ascertained, yet been recorded. The peculiar mental syndrome presented by patients with pernicious anæmia, though very uncommon, in the early stages at least (in Minot's last 100 cases, in only one was the disease initiated by mental symptoms), is quite characteristic. It has been well described recently by Phillips (14), McAlpine (26), Hackfield (27), Piney (28), Francke (29), and Atkin (30).

In the example to be recorded, the mental symptoms preceded recognition of the particular form of anæmia. The real interest of this case lay in the fact that although mental symptoms had been present for several years, they had not been considered in relation to the gastrectomy performed in 1923 and to the subsequent onset of anæmia. An anæmia had been diagnosed before the patient was admitted to hospital and liver treatment had been instituted, but this treatment, in the absence of the essential gastric factor, would seem to have been ineffective. It was difficult to estimate how long anæmia had really been present, but from the history it must be assumed that mental symptoms antedated the onset of the anæmia. Suspicion of a nervous lesion also in this case was aroused by the symptom of numbness in the soles of the feet and decreased vibratory sense, but repeated examination of the nervous system would be necessary in such a case before the diagnosis of subacute combined degeneration of the cord could be reached with certainty.

CASE 3.—Mrs. D—, æt. 49, was admitted to St. Andrew's Hospital on August 7, 1934, as a voluntary boarder. There was a history of loss of emotional control for some years, which had latterly been succeeded by a gradual development of phobias (e.g., claustrophobia), and ideas suggestive of religious exaltation. These symptoms had been exacerbated by the menopause, which occurred three years prior to admission.

Gastric symptoms over a lengthy period culminated in the necessity for an operation in 1923, at which an hour-glass stomach was found. A Polya gastrectomy was then performed with satisfactory results, there being no return of abdominal pain.

At the beginning of 1933 the patient had an acute illness, the exact nature of which was undetermined. There was, however, generalized œdema with ascites, and the abdomen was tapped on three occasions. The patient herself had but a faint memory of this illness.

The salient features of the examination on admission were as follows:

The patient was a pale, rather frail-looking woman, 5 ft. 8 in., and weighed 7 st. 9 lb. Muscular tone was generally poor. The scar of a paramedial incision was present on the abdomen. Tongue clean, smooth, with loss of papillæ and some glossitis at tip; edentulous; mucous membranes pale. Blood-pressure 102 systolic, 60 diastolic. Cardio-vascular system normal except for a hæmic murmur heard at the apex. No abnormalities detected in the lungs. Liver and spleen not palpable. Nervous system: vision in right eye said to be poorer than that in left. On ophthalmoscopic examination a high degree of myopia was found. The discs were normal except for a myopic crescent in the right eye. The ocular movements were full and equal, and the functions of the other cranial nerves were normal. Power was equally poor in both arms and both legs. There were no gross sensory changes, but vibration was poorly appreciated on both feet. (Numbness on the soles of the feet was complained of.) The arm-jerks, knee-jerks and ankle-jerks were present and equal. The plantar responses were flexor.

Mentally there was grave loss of emotional control with loss of judgment. There were no definite delusions of persecution, but the "persecution tendency" was adequately demonstrated by the patient's habit of making scenes over trifles, real or imaginary; in these scenes she was always in the right, but had been "put in the wrong by others", especially by those about her. She had a pronounced fear of being left alone, particularly in a room with the door closed. No hallucinations were present. The dominant feature of the patient's mental state was self-pity, which was increased by any display of sympathy on the part of those in charge of her.

Laboratory findings: Blood-count, August 9: Red blood-cells 3,648,000 per c.mm., hæmoglobin 77·7%, colour index 1·07, white blood-cells 5,700 per c.mm., polymorphonuclears 44%, large lymphocytes 26·5%, small lymphocytes 22·5%, monocytes 5·5%, eosinophils 1·5%. Marked anisocytosis and poikilocytosis; many macrocytes and microcytes seen; slight polychromasia; one nucleated red cell seen whilst counting 200 white cells. Rough halometric reading showed a megalocytosis. Van den Bergh reaction negative; Kahn reaction negative in blood. A test-meal on August 13 disclosed a complete achylia gastrica. No blood was present in any sample. Culture of the resting juice gave a copious growth of *Streptococcus salivarius* and *Streptococcus pyogenes*. From the stools were cultured only *Bacillus coli*, *Streptococcus fæcalis* and a leptothrix. A glucose tolerance test showed a diminished tolerance with passage of sugar in the one- and two-hour specimens of urine.

From August 17 to August 20 the patient was given 10 grm. of ventriculin three times a day, and from August 20 to 23 this was increased to 40 grm. per diem. By this date there was already some improvement in the physical condition.

A blood-count on August 23 was indicative: Red blood-cells 4,448,000 per c.mm., hæmoglobin 74·1%, colour index 0·84, white blood-cells 7,500 per c.mm., polymorphonuclears 72%, large lymphocytes 5%, small lymphocytes 18%, monocytes 3%, eosinophils 1·5%, basophils 0·5%. Anisocytosis and poikilocytosis marked; many macrocytes and microcytes; two nucleated red cells seen whilst counting 200 white cells; reticulocytes 1·5%; average diameter of the red cells (halometric method) 8·5μ.

Mentally the patient was showing more insight into her condition. Two days later, unfortunately, she was transferred to other care.

This case illustrates well the statement of Rowlands and Simpson, that not all the features of pernicious anæmia are reproduced in the post-operative form. They found that the Van den Bergh reaction was usually within normal limits, and that megaloblasts were seldom present. In this case no megaloblasts could be seen and the Van den Bergh reaction was negative. The other

features of the blood-picture were typical of pernicious anæmia, and the opportunity was fortunately available at this time of measuring approximately the average diameter of the red cells, the cardinal point in diagnosis of pernicious anæmia.

The amount of recovery which took place (of which we were advised on inquiry after the patient had left St. Andrew's Hospital) was considerable. A blood-count done a month later by Dr. Fraser, of Bristol (which was kindly furnished by Dr. Parkes, also of Bristol), " showing no evidence of pernicious or other anæmia ", bore witness to the efficacy of treatment by ventriculin.

The following case of pernicious anæmia is briefly presented for comparison with the last case :

CASE 4.—(The clinical features of this case are merely indicated, as they are to be published in detail by Dr. N. R. Phillips, through whose courtesy this abstract from his notes has been made.)

Miss R—, æt. 42, was admitted to St. Andrew's Hospital on December 8, 1932. She was hypochondriacal and introspective, and had delusions of being persecuted by her family and by those around her. There was loss of emotional control, and an inordinate craving for sympathy. These symptoms had been progressively evident 1or the past five years. Three years before admission the patient had begun to complain of heaviness of the legs and a " cold feeling round the lower part of the stomach and the legs ", and latterly, of loss of power in the hands and feet.

Examination on admission showed a tall, rather emaciated woman, with a yellowish colour, who weighed 8 st. 8 lb. The tongue was devoid of papillæ and displayed a severe glossitis. The few remaining teeth were septic. No abnormalities were detected in either the cardiovascular or respiratory systems. Nervous system : Cranial nerves normal. Gait ataxic. Muscular power fair in arms and legs. Sense of position impaired in all limbs ; pin-prick well appreciated, but some diminution of light touch over both legs. Arm-jerks, knee-jerks and ankle-jerks absent. Plantar response : Right extensor, left doubtful. The diagnosis of subacute combined degeneration of the cord associated with pernicious anæmia was confirmed by a blood-count on the same day.

Laboratory investigations : Blood-count, December 8. Red blood-cells 3,208,000 per c.mm., hæmoglobin 57%, colour index 0·9, white blood-cells 4,600 per c.mm., polymorphonuclears 63%, large lymphocytes 11·5%, small lymphocytes 21%, monocytes 3·5%, basophils 1%. Marked poikilocytosis and anisocytosis with megalocytes predominating ; marked polychromasia. One nucleated red cell seen whilst counting 200 white cells. Hypersegmentation of polymorphonuclears. Complete achylia gastrica was revealed by a test-meal on December 23. Examination of cerebro-spinal fluid : Cells, 1 per c.mm. ; total protein, 0·05% ; Nonne-Apelt and Pandy negative ; Lange negative, Kahn reaction negative.

Treatment by whole liver and ferruginous serum was instituted, resulting in steady improvement in the physical and mental condition and a corresponding improvement in subsequent blood-pictures.

January 4, 1933 : Red blood-cells 3,560,000 per c.mm., hæmoglobin 56·4%, colour index 0·8, white blood-cells 4,200 per c.mm., polymorphonuclears 61·5%, large lymphocytes 15%, small lymphocytes 19·5%, monocytes 2%, eosinophils 0·5%, basophils 1·5%. Marked poikilocytosis ; many large forms of red cell present ; 3 nucleated red cells seen whilst counting 200 white cells.

January 24 : Red blood-cells 3,512,000 per c.mm., hæmoglobin 59·4%, colour index 0·85, white blood-cells 7,800 per c.mm., polymorphonuclears 55%, large lymphocytes 30%, small lymphocytes 10%, monocytes 3%, basophils 2%. Much anisocytosis, megalocytes predominating ; little poikilocytosis ; 2 nucleated red cells seen.

February 8: Red blood-cells 3,696,000 per c.mm., hæmoglobin 64·7%, colour index 0·9, white blood-cells 4,900 per c.mm., polymorphonuclears 54%, large lymphocytes 19%, small lymphocytes 25%, monocytes 2%. Marked anisocytosis with many megalocytes. No nucleated red cells seen.

March 20: Red blood-cells 3,832,000 per c.mm., hæmoglobin 67%, colour index 0·9, white blood-cells 2,800 per c.mm., polymorphonuclears 54·5%, large lymphocytes 15·5%, small lymphocytes 24%, monocytes 4%, basophils 2%. Slight poikilocytosis and anisocytosis; 2 nucleated red cells seen.

April 12: Red blood-cells 4,144,000 per c.mm., hæmoglobin 64·7%, colour index 0·8, white blood-cells 5,300 per c.mm., polymorphonuclears 61·5%, large lymphocytes 8%, small lymphocytes 27%, monocytes 3%, basophils 0·5%. Much anisocytosis with megalocytes predominating. Slight polychromasia, poikilocytosis and punctate basophilia; 2 nucleated red cells seen.

May 9: Red blood-cells 4,560,000 per c.mm., hæmoglobin 77·6%, colour index 0·86, white blood-cells 5,300 per c.mm., polymorphonuclears 69·5%, large lymphocytes 11%, small lymphocytes 14%, monocytes 5%, basophils 0·5%. Slight anisocytosis and poikilocytosis. No nucleated red cells seen.

June 8: Red blood-cells 3,664,000 per c.mm., hæmoglobin 67%, colour index 0·93, white blood-cells 6,200 per c.mm., polymorphonuclears 59%, large lymphocytes 22%, small lymphocytes 15%, monocytes 3%, basophils 1%. Much anisocytosis, poikilocytosis and polychromasia; 2 nucleated red cells seen.

June 21: Red blood-cells 4,864,000 per c.mm., hæmoglobin 77·6%, colour index 0·8, white blood-cells 8,000 per c.mm., polymorphonuclears 58%, large lymphocytes 28%, small lymphocytes 11·5%, monocytes 2·5%. Slight anisocytosis and poikilocytosis. No nucleated red cells seen.

Removal of septic teeth on June 7, 1933, was followed by a severe hæmorrhage from the gums, which caused a temporary set-back, as indicated by the blood-picture on June 8. Following the hæmorrhage, liveroid, ½ drm., and 20 gr. of Blaud's pill three times a day were substituted for the whole liver. Subsequent recovery was rapid, and on August 5 the patient was discharged from hospital mentally well and greatly improved physically.

The chief feature of this case was the severity of the nervous symptoms, and the remarkable amount of recovery of power of movement with improvement gait which ensued as a result of liver treatment by mouth, with a concomitant improvement in the blood-picture.

Summary.

A series of 300 psychotic patients was investigated with reference to the occurrence of achlorhydria as compared with normal individuals. 10·6% were found to be achlorhydric by the fractional test-meal method. This percentage was 4% lower than that recorded by other observers for large numbers of healthy people of approximately the same age.

The conclusion was therefore reached that achlorhydria does not occur more commonly amongst psychotics than amongst the sane.

The incidence of achlorhydria in relation to age was considered.

There was no preponderancy of achlorhydria in any particular psychosis, the higher percentage apparently occurring in states of depression being due to the greater age of patients exhibiting this psychosis.

Reference was made to different forms of anæmia associated with achlorhydria and their relative incidence.

Of the six cases of hyperchromic anæmia encountered in this series, four have been reported in some detail.

Two of these presented a form of hyperchromic anæmia occurring in the senium, distinct from, and unrelated to, pernicious anæmia, though usually responding to the same treatment.

A case of pernicious anæmia with mental symptoms following a gastrectomy ten years previously has been recorded, together with a brief abstract, for comparison, of another case of pernicious anæmia with mental symptoms.

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