DIETARY TREATMENT OF HYPERTENSION

BY

H. UCKO, M.D.

Until recently there was a general consensus that hypertension was not benefited by diet unless it was due to or accompanied by renal disease or obesity. Kempner (1944a, 1944b, 1945, 1946, 1948) produced evidence that a diet consisting of rice, fruit, and sugar without the addition of other foodstuffs led to a reduction of the mean blood pressure by more than 20 mm. in 62% of cases of hypertension and caused marked improvement of the symptoms and signs of hypertensive disease. In some patients small amounts of non-leguminous vegetables, potatoes, lean meat, and fish can be added later, but this is often followed by a rise in blood pressure, which always occurs on return to normal food. Yet prolonged adherence to the strict diet may lead to a negative nitrogen balance (Schwartz and Merlis, 1948).

These results have in part been confirmed (Flipse and Flipse, 1947; Canter, 1948; Contratto and Rogers, 1948). In Page, Corcoran, and Taylor's (1949) series less than 20% of cases improved. The diet has also been found effective in dogs with experimental hypertension (Dick and Schwartz, 1947).

Some authors have attributed the results of the rice diet to starvation. If 10 oz. (280 g.) of rice and 5-6 oz. (140-170 g.) of sugar are eaten daily the caloric intake can be kept up to 2,000. Yet many patients prefer insufficient calories to the full ration. Starvation can reduce normal and high blood pressure (Lups and Francke, 1947; Brozek, Chapman, and Keys, 1948); this effect has been attributed to the deficient protein intake.

Kempner's rice diet contains as little as 150 mg. of sodium a day. It has experimentally been found that sodium chloride administration potentiates the hypertensive effect of deoxycortone (D.C.A.), while animals on a salt-free diet show no or a greatly reduced response (Knowlton, Loeb, Stoerk, and Seegal, 1947). On the other hand, sodium restriction is capable of reducing the blood pressure of hypertensive rats, and such animals choose a diet with a low sodium content (*Yearbook of Endocrinology, Metabolism, and Nutrition*, 1948). In the chicken, hypertension and reversible renal changes have been produced by the mere addition of salt to the drinking-water (Lenel, Katz, and Rodbard, 1948). It has been shown that the action of salt is due to its sodium ion (Friedman, Friedman, and Polley, 1948).

In human beings the pressor effect of D.C.A. on hypertensives (Perera, 1945; Goldman and Schroeder, 1948) can similarly be prevented by rigid salt restriction (Perera, 1945). While the addition of salt does not affect the blood pressure of normal people (Grant and Reischman, 1946), Goldzieher and Salmovitz (1943) observed salt retention in hypertensives and decrease in blood pressure after salt restriction and ammonium chloride medication. The latter is capable of preventing the effects of D.C.A.-overdosage in animals (H. Selye, 1946) and returns to normal the increased Na/Cl ratio in the serum of D.C.A.-treated animals (F. L. Selye, 1947). An increased Na/Cl ratio was found by the last-named author also in the blood of some hypertensive patients with high diastolic pressures, and Goldzieher and Stone (1949) have shown that sodium and chloride can be retained independently of each other. There is no other reliable evidence for the existence of sodium retention in

essential hypertension, but Perera (1947) observed that the reaction of hypertensives to salt restriction differs from that of normal subjects.

The value of sodium restriction in the treatment of congestive heart failure and oedema has been established (Bridges, Wheeler, and White, 1946; Wheeler, Bridges, and White, 1947; Peters, 1948). Grollman (1946) reported good results in hypertensive disease from a diet with less than 500 mg. of sodium a day but not from moderate sodium restriction. Perera (1947) observed a decrease of the "resting" blood pressure by a diet containing 280-320 mg. of sodium. Bryant and Blecha (1947) found the disappearance of symptoms and a fall in pressure to or below 155/95 in 20% of cases on a diet containing 200 mg. of sodium. Successes were also reported by Rosenberg, Rosenthal, and Rosenbluth (1948) and by Schroeder (1948). Bang, Bechgaard, and Nielsen (1949) observed a decrease of blood pressure in 16 out of 26 patients with hypertension on a diet with less than 400 mg. of sodium. The addition of salt caused renewed rise of the pressure. In one case of chronic nephritis salt deprivation led to uraemia.

Present Investigation

Kempner's rice diet, a barley diet, and a low-sodium diet were tested on 14 unselected cases of hypertension—3 men and 11 women. The ages ranged from 35 to 72 years, the mean age being 54.5. Two patients, a man and a woman (Cases 6 and 9), suffered from chronic renal disease with albuminuria, cylindruria, and azotaemia; the male patient was also a moderate diabetic and had a trophic ulcer of the toe. The youngest female patient was a typical case of Cushing's syndrome. All other patients suffered from essential hypertension. In all cases hypertension had been present for many years.

The observation periods varied from one to eleven months. Only the "casual" blood pressures were recorded, as all patients were ambulatory and continued with their normal activities. No rest or change of life was enforced. Blood-pressure readings were taken on the same arm with the patient in the same position, and the mean value of four readings was recorded. When the blood pressure had not been observed for a long time before treatment, preliminary blood-pressure estimations were made on at least three different occasions. As an index of the sodium chloride intake the urinary chloride excretion was determined once a week. In cases with renal disturbances the blood urea was estimated before and during treatment. All patients were clinically examined and records of their heart silhouettes were taken at intervals.

Six patients were put on the rice diet; five of them continued on the low-sodium diet, one after an interval of several months. Four of the five patients on the barley diet continued with the low-sodium diet. Four patients were put on the low-sodium diet from the beginning.

Diets

1. Kempner's rice diet was used in its original form.

2. A barley diet was given which was identical with the rice diet, except that rice was replaced by pearl barley. According to McCance and Widdowson (1946), from whose publication the figures in this paper have been taken, pearl barley contains 2.6 mg. of sodium per 100 g., while rice contains 6.3 mg. per 100 g.

3. The following low-sodium diet was used. All food must be prepared without salt, and no self-raising flour, baking powder, or sodium-containing medicine must be taken.

TABLE I.—*Low-sodium Diet*

Daily Menu	Calories	Sodium (mg.)
Meat, 100 g. (raw weight) ..	190-250	40-90
(or Fish, 75 g., raw weight) ..	(70-100)	(75-90)
Bread, unsalted, 150 g. ..	390	4-6*
Fruit, 1½-2 lb. ..	250-300*	(18) 12-16 (24)
Vegetables, 360 g. (containing less than 6 mg. of Na per 100 g.) ..	20-160	Trace-24
Potatoes, 125 g. (preferably old) ..	100	4
Rice, barley, or tapioca, 100 g. ..	360	2.5-6
(or Semolina, 50 g.) ..	(176)	
Butter or margarine, 30 g. (unsalted) ..	240	3-11 (?)
Lard, 15 g. ..	135	Trace
Olive oil, 15 g. ..	140	
Milk, 60 g. ..	40	30
(or Cream, 90 g.) ..	(360)	(28)
Honey, jam, or marmalade, 15 g. ..	40	1.6-2
Sugar, 30-60 g. ..	120-240	Trace
Egg, one (preferably not more than four times a week) ..	85	70
	1,800-2,400	156-262

* Approximate amounts.

Results

Some fall in blood pressure occurred in all patients, but the extent varied. Tables II and III illustrate the findings. Five patients were on the rice diet for three to six weeks, one for almost three months. Cases 1-4 had essential hypertension, Case 5 suffered from Cushing's syndrome, and Case 6 had chronic renal disease with azotaemia (blood urea, 90 mg. in 100 ml.). In only two patients (Cases 4 and 6) did the blood pressure reach approximately normal levels, though the diastolic pressure remained slightly above normal. One was the patient with chronic nephritis and diabetes mellitus; his preliminary fasting blood sugar was 375 mg. in 100 ml., and the carbohydrates of the diet were covered by 32 units of globin insulin. The other patient had essential hypertension, no cardiac dilatation or ocular changes, but minimal albuminuria and slight oedema of the ankles. The variable loss of weight which occurred in the patients of this group bore no relation to the extent of the fall in blood pressure, but seemed to be greater in over-weight patients.

Comparable results were obtained in patients on the barley and low-sodium diets, except that the loss of weight

TABLE III

Case No.	Rice (R) or Barley (B) Diet		Low-sodium Diet			
	Duration (Weeks) and Nature of Diet	Mean B.P.	Duration of Diet (Weeks)	Mean B.P.	Weight	
					Before Diet	After Diet
7	5 (B)	220 / 97.5	25	214 / 95	1b. 134 (60.8)	1b. 134 (60.8)
9	4 (B)	217.5 / 114	3	218 / 109	143½ (65.1)	143½ (65.1)
8	9½ (B)	190 / 117	16	177 / 111	108 (49)	108 (49)
1	5½ (R)	180 / 128	25	176 / 119	153½ (69.6)	153½ (69.6)
2	4½ (R)	163 / 110	6	166 / 105	158½ (71.9)	158½ (71.9)
4	6 (R)	120 / 90	36	125 / 95	159 (72.1)	159 (72.1)
11	6 (B)	142.5 / 89	7?	169 / 106	115½ (52.4)	115½ (52.4)
6	3 (R)	133 / 94	3	135 / 84	178 (80.7)	178 (80.7)
Mean values		170.7 / 104.9		172.5 / 103		

was less marked in the latter group. Case 3 had normal food for five months after the rice diet. The blood pressure had risen to an average of 200/113 when the patient started the low-sodium diet. The average fall in blood pressure of the patients on the barley diet was higher than it was on the low-sodium diet and lower than on the rice diet, but the number of patients in each group is far too small for general conclusions to be drawn from these figures.

Table III shows the results obtained by the low-sodium diet in patients who started on the rice or barley diet and continued on the low-sodium diet. It is evident that the blood pressures of all the eight patients in this group were maintained satisfactorily; in most of them the pressure decreased even further. Case 11, the only one showing a rise in blood pressure, did not adhere strictly to the diet. She was the second case of chronic nephritis and showed marked improvement in general health; urinary protein and cylindruria decreased considerably, the blood urea fell from 150 to 50 mg. in 100 ml., and retinopathic changes of the ocular fundus regressed. All patients, except Case 7, felt better, oedema and slight albuminuria disappeared if present, and the heart size decreased slightly in patients with cardiac dilatation. The blood urea in Case 6 remained unchanged; his albuminuria diminished considerably, his fasting blood sugar dropped to 165 mg. in 100 ml., and the

TABLE II

Case No.	Sex	Age	Diagnosis	Duration of Diet (Weeks)	Weight		Mean B.P. Before Diet		Mean B.P. During Diet		Decreased B.P.		Decrease in " Mean " Pressure: $\frac{1}{2}(\text{Syst.} + \text{Diast.})$	Decrease of Initial Pressure	
					Before Diet lb. kg.	Loss on Diet lb. kg.	Systol.	Diastol.	Systol.	Diastol.	Systol.	Diastol.		Systol.	Diastol.
Rice Diet															
1	F	46	Essential hypertension	5½	164 (74.4)	10½ (4.8)	240	137	180	128	60	9	34.5	25.0%	6.5%
2	M	66	" "	4½	165 (74.8)	6½ (2.9)	213	135	163	110	50	25	37.5	23.5%	18.5%
3	F	57	" "	11½	122 (55.3)	2½ (1.1)	210	118	163	98	47	20	33.5	22.4%	17.0%
4	M	49	" "	6	171 (77.6)	12 (5.4)	190	135	120	90	70	45	57.5	37.0%	33.3%
5	F	35	Cushing's syndrome	3	285 (129.3)	20 (9.1)	200	115	160	98	40	17	28.5	20.0%	15.0%
6	M	52	Chronic nephritis; diabetes	3	188 (85.3)	10 (4.5)	195	118	133	94	62	24	43.0	31.8%	20.3%
Mean values:							208	126.3	153	103	55	23.3	39.1	26.6%	18.4%
Barley Diet															
7	F	68	Essential hypertension; rheumatoid arthritis	5	140 (63.5)	6 (2.7)	267.5	112.5	220	97.5	47.5	15	31.2	17.8%	13.3%
8	F	49	Essential hypertension; lower body obesity	9½	122 (55.3)	14 (6.4)	254	135	190	117	64	18	41.0	25.0%	13.3%
9	F	59	Essential hypertension	4	152 (68.9)	8½ (3.9)	250	134	217.5	114	32.5	20	26.2	13.0%	15.0%
10	F	59	" "	3	164 (74.4)	2½ (1.1)	206.5	105	171	98	35.5	7	21.2	17.1%	6.6%
11	F	51	Chronic nephritis	6	122 (55.3)	6½ (2.9)	234	120	142.5	89	91.5	31	61.2	39.1%	25.8%
Mean values:							242.4	121.3	188	103.1	54.2	18.2	36.2	22.4%	14.8%
Low-sodium Diet															
3	F	57	Essential hypertension	22	126 (57.2)	2½ (1.1)	202	113	170	98	32	15	23.5	15.8%	13.3%
12	F	65	" "	7	101 (45.8)	2 (0.9)	205	105	175	92	30	13	21.5	14.6%	12.3%
13	F	59	" "	8½	162 (73.5)	3 (1.4)	197.5	107.5	167.5	91	30	16.5	23.2	15.2%	15.3%
14	F	73	" "	7½	163 (73.9)	4 (1.8)	205	107.5	157	93	48	14.5	31.2	23.4%	13.5%
Mean values:							202.4	108.2	167.4	93.5	35	15	24.9	17.5%	13.6%

ulcer of the toe healed. No signs of salt deprivation were observed, but some patients felt slightly weak at times; extreme coldness and blanching of fingers and toes occurred in two patients, and one patient (Case 4) had two attacks of faintness when the blood pressure was very low and the pulse pressure dropped to 25 mm. Gastric upsets occurred in several patients on the rice diet.

Two major incidents occurred which may not be related to the treatment. Patient 9 developed melaena after she had been on the barley diet for four weeks and on the low-sodium diet for three weeks. A cause for the bleeding was not found, but the diet was discontinued. Patient 2, who never kept rigidly to his diet and whose urinary chloride excretion ranged between 120 and 170 mg. per 100 ml., as compared with 20–60 mg. per 100 ml. in people who adhered strictly to the diet, had a coronary thrombosis 40 days after his return to normal food and died as the result of the thrombosis seven weeks later.

The results obtained from the low-sodium diet are of special interest, as it supplies an adequate amount of protein and includes leguminous vegetables and fat, which, according to Kempner, upset the effect of his diet.

A close scrutiny of the menus and the chloride excretion of the patients showed that the lowest observed blood-pressure levels were maintained only with a daily intake of under 250 mg. of sodium. It is also important to realize that the tendency of the hypertensive blood pressure to vary unduly during the day remains unchanged and that morning and evening pressures may therefore diverge considerably. The Chart illustrates these points. It is a typical example

Chart showing blood-pressure readings in Case 4 (essential hypertension of many years' standing).

of the influence of dietary treatment, and shows the morning (not the resting) pressures of the best- and longest-observed patient (Case 4), and some of his afternoon pressures in comparison.

Discussion

The results indicate that the described diets are effective in reducing the blood pressure in hypertensive disease and in chronic renal disease, and they suggest that it is chiefly the low sodium content which is responsible for this effect. The fall in blood pressure is usually accompanied by improvement or disappearance of the hypertensive symptoms and signs and by improvement in general health. Though only a small number of patients seem to respond with normalization of the pressure, it appears that improvement of the hypertension is beneficial to the patient's health.

The figures in Tables II and III show that the systolic pressure after treatment was still well over 200 mm. in two patients and the diastolic pressure over 110 in two others. If one considers the wide daily variations and the effects of small deviations from the strict diet, it appears that only a certain number of patients will benefit enough from

sodium restriction to warrant the institution of a regimen that can be upheld only with great personal and social inconvenience. In patients who respond well, however, sodium restriction may have important therapeutic consequences. It has benefited patients after unsuccessful sympathectomy (Bryant and Blecha, 1947) and may well be tried in selected cases before operation is considered. Decisive successes cannot usually be expected from mere salt restriction: the daily intake of sodium must not exceed 200 to 250 mg. The low-sodium diet is the diet of choice, as it provides the full supply of essential foodstuffs and so can be maintained for a long time; rice or barley diets can be included.

The effect of sodium restriction on hypertension may have great theoretical significance. It appears that the body needs sodium for the production of hypertension and that its withdrawal may create a metabolic situation in which high blood pressure cannot be properly maintained. Sodium drainage may be the cause of the hypotension in Addison's disease. Black (1946) found hypotension, low serum sodium values, and an undue loss of sodium in the faeces in some cases of tropical and non-tropical sprue. Conversely, there is a tendency towards sodium retention in pregnancy toxæmia, in not too advanced chronic nephritis, and also in some cases of Cushing's syndrome; and drastic sodium restriction benefits the hypertension of all these conditions.

There is a striking similarity between D.C.A. intoxication and such diseases as essential hypertension, pregnancy toxæmia, and Cushing's syndrome. The part played by the sodium metabolism in these conditions favours the hypothesis that overproduction of adrenal mineralocorticosteroids may be one of their essential features. H. Selye (1946) has shown that "diseases of adaptation" may originate from a faulty mechanism of adaptation to un-specific damaging stimuli, and that overproduction of adrenal corticosteroids under pituitary stimulation constitutes one of the most important physiological events in the defence mechanism of the body. It is therefore conceivable that intoxication of the body with adrenal mineralocorticosteroids may occur as a result of maladaptation and that deficiency or loss of sodium may prevent or mitigate such an intoxication in the same way as it lessens the effect of D.C.A. intoxication. That sodium restriction does not affect the neurogenic component of hypertension is borne out by the observation that external and emotional stimuli influence the blood pressure of a patient who has responded to diet in the same way as that of an untreated hypertensive.

Summary

The results of Kempner's rice-fruit-sugar diet, of a barley diet, and of a low-sodium diet on 14 unselected cases of hypertension are described.

It is suggested that the effect of Kempner's rice diet is mainly due to its low sodium content.

The clinical effect of sodium restriction on hypertension and its theoretical consequences are discussed.

REFERENCES

- Bang, H. O., Bechgaard, P., and Nielsen, A. (1949). *British Medical Journal*, **2**, 1203.
- Black, D. A. K. (1946). *Lancet*, **2**, 671.
- Bridges, W. C., Wheeler, E. O., and White, P. D. (1946). *New Engl. J. Med.*, **234**, 573.
- Brozek, J., Chapman, C. B., and Keys, A. (1948). *J. Amer. med. Ass.*, **137**, 1569.
- Bryant, J. M., and Blecha, E. (1947). *Proc. Soc. exp. Biol., N.Y.*, **65**, 227.
- Canter, H. E. (1948). *Penn. med. J.*, **51**, 1411.
- Contratto, A. W., and Rogers, M. B. (1948). *New Engl. J. Med.*, **239**, 531.

- Dick, G. F., and Schwartz, W. B. (1947). *Proc. Soc. exp. Biol., N.Y.*, **65**, 22.
- Flipse, M. E., and Flipse, M. J. (1947). *Sth med. J.*, **40**, 721.
- Friedman, S. M., Friedman, C. L., and Polley, J. R. (1948). *Amer. J. Phys.*, **153**, 226.
- Goldman, M. L., and Schroeder, H. A. (1948). *Science*, **107**, 272.
- Goldzieher, J. W., and Stone, Gilbert C. H. (1949). *J. clin. Endocrinol.*, **9**, 368.
- Goldzieher, M. A., and Salmovitz, S. (1943). *Ibid.*, **3**, 37.
- Grant, H., and Reischman, F. (1946). *Amer. Heart J.*, **32**, 704.
- Grollman, A. (1946). *J. Amer. diet. Ass.*, **22**, 864.
- Kempner, W. (1944a). *N. C. med. J.*, **5**, 125, 273.
- (1944b). *J. Amer. med. Ass.*, **125**, 48, 60.
- (1945). *N. C. med. J.*, **6**, 61, 117.
- (1946). *Bull. N.Y. Acad. Med.*, **22**, 358.
- (1948). *Amer. J. Med.*, **4**, 545.
- Knowlton, A. I., Loeb, E. N., Stoerk, H. C., and Seegal, B. C. (1947). *J. exp. Med.*, **85**, 187.
- Lenel, R., Katz, L. N., and Rodbard, S. (1948). *Amer. J. Phys.*, **152**, 557.
- Lups, S., and Francke, C. (1947). *Acta med. scand.*, **126**, 449.
- McCance, R. A., and Widdowson, E. M. (1946). "The Chemical Composition of Foods," *Spec. Rep. Ser. med. Res. Coun.*, No. 235. H.M.S.O., London.
- Page, I. H., Corcoran, A. C., and Taylor, R. D. (1949). *Postgrad. Med.*, **5**, 211.
- Perera, G. A. (1945). *J. Amer. med. Ass.*, **129**, 537.
- (1947). *Conn. med. J.*, **11**, 963.
- Peters, J. P. (1948). *New. Engl. med. J.*, **239**, 353.
- Rosenberg, B., Rosenthal, A. E., and Rosenbluth, M. B. (1948). *Amer. J. Med.*, **5**, 815.
- Schroeder, H. A. (1948). *Ibid.*, **4**, 578.
- Schwartz, W. B., and Merlis, J. K. (1948). *J. clin. Invest.*, **27**, 406.
- Selye, F. L. (1947). *Canad. med. Ass. J.*, **57**, 325.
- Selye, H. (1946). *J. clin. Endocrinol.*, **6**, 117.
- Wheeler, E. O., Bridges, W. C., and White, P. D. (1947). *J. Amer. med. Ass.*, **133**, 16.
- Yearbook of Endocrinology, Metabolism, and Nutrition* (1948), p. 354.

EFFECT OF VITAMIN B₁₂ ON NEUROPATHY IN PERNICIOUS ANAEMIA TREATED WITH FOLIC ACID

BY

H. FULD, M.D., M.R.C.P.

Physician, Newsham General Hospital, Liverpool

The remarkable effectiveness of vitamin B₁₂ in severe lesions of the central nervous system caused by folic-acid treatment of pernicious anaemia is well illustrated by the record of a patient who came recently under observation.

Case Report

A woman aged 74, whose previous history was one of good health, developed lassitude and dyspnoea on exertion about three years ago, when pernicious anaemia was diagnosed and confirmed by blood examination. Concentrated liver injections were given. After the third injection she developed a sensitization dermatitis, for which she was admitted to the skin department of a hospital on February 15, 1948—that is, four months after the onset of the skin disease. Apart from the dermatitis she appeared to be in good health and the case report did not record any neurological disorder. Her blood count on February 18 was: red cells, 3,690,000; white cells, 8,650; haemoglobin, 80%; colour index, 1.1. Her skin condition cleared up with local application and x-ray therapy, and she left hospital on February 25 with a haemoglobin level of 99%. Whilst in hospital, liver injections were stopped and she was put on 15 mg. of folic acid daily, which she had taken until her admission to this hospital.

In May, 1949 (after 15 months' folic-acid treatment), she complained of weakness and unsteadiness of her legs and loss of appetite. From August her diet consisted of bread, margarine, butter, and tea. She had an egg on rare occasions, but took practically no vegetables, meat, or fish. Towards the middle of October she became mentally deranged, bed-ridden, and incontinent.

On admission to the medical division of Newsham Hospital on November 8 her condition was as follows. She lay in a curled-up position, unable to give any history. She was disorientated about place and time, extremely restless, incontinent, delusional, and very dirty in her habits. There was no gross wasting. The skin was dry, with a scaly papular dermatitis of the lower third of both legs. There was angular stomatitis, and the tongue was glazed and beefy. The lymph nodes were not enlarged. Fibrillation was present. B.P. 90/60; chest clear. There was no enlargement of liver or spleen and no tenderness or any mass in the abdomen. The urine was normal. A blood count showed: red cells, 3,500,000; haemoglobin, 78%; colour index, 1.1; M.C.D., 7.8 μ (Eve). White cells, 4,000; lymphocytes 2,150 (54%), monocytes 50 (1%), polymorphonuclears 1,700 (42%), eosinophils 100 (3%). The blood film was consistent with treated pernicious anaemia.

Examination of the nervous system revealed no disorder of the cranial nerves, and the fundi were normal. Investigation of the upper limbs showed gross ataxia, brisk tendon reflexes, Hoffmann's sign present on left side, impaired superficial sensation, joint and vibration sense lost, and muscular power not grossly impaired; the abdominal reflexes were absent. The lower limbs showed gross ataxia, brisk tendon reflexes, bilateral extensor response, impaired muscular power, loss of vibration sense and joint sense, impaired sensation for touch and pain.

A diagnosis was made of neuropathy following folic-acid treatment of pernicious anaemia in a woman who also suffered from nutritional (vitamin B) deficiency.

On November 15, 2 ml. of "cytamen," containing an equivalent of 40 μ g. of vitamin B₁₂, was injected. Subsequently 1 ml. was injected every third day until December 1, every fifth day until December 13, and every seventh day afterwards until February 28, 1950, when she was put on fortnightly injections of 2 ml. The total dose of vitamin B₁₂ given was 0.5 mg.

Progress.—For five days she had to be fed on fluids only. Her appetite returned after the second injection. She remained incontinent until December 12, by which time she could sit on a chair. Towards the end of December walking exercises were started. On January 5 the ataxia of her upper limbs had disappeared. The reflexes of her lower limbs were still brisk and there was an extensor response on the left side. Superficial and deep sensation were both impaired in her legs. Her mental condition had greatly improved, and she was able for the first time to give a clear history of herself except for the period after August, 1949.

On January 21 the case record states: "Mentally alert and rational; lively sense of humour. Upper limbs—no weakness of either hand. Reflexes brisk; no impairment of superficial or deep sensations; vibration sense normal. Finger-nose test normal. Lower limbs—brisk tendon reflexes. Bilateral flexor response—some impairment of sensation to cotton-wool and pin-prick. No loss of muscular or joint sense. Vibration sense absent. Heel-knee attempt still poor. Gait unsteady but not spastic."

On February 7 she walked without help and was quite steady. There was still some impairment of deep sensation. On February 14 she walked quite normally and climbed two flights of stairs unaided. Her physical and mental condition was good. Blood examination showed normal values from December 13 onwards. The patient left hospital in March with a recommendation to her doctor for maintenance doses of 40 μ g. vitamin B₁₂ every fortnight.

Discussion

The above case record confirms the dangers of folic-acid treatment of pernicious anaemia pointed out by Israëls and Wilkinson (1949). The patient, who had had no previous neurological lesion, developed a severe neuropathy involving the brain, spinal cord, and peripheral nerves, in the fifteenth month of folic-acid treatment, during which period her blood remained at a fair level. The resulting psychosis and the neurological lesions were promptly arrested by