

determine by observation the amount of cooling needed to produce a lesion in a chilblain subject ; for in no experiment can we be sure of the extent of preliminary damage that is present: the final or provocative cooling may be regarded as adding its quota of damage, the sum of which leads to an obvious reaction.

We are brought to ask if there is evidence that cooling can produce chronic inflammatory lesions in skin that has previously displayed no chilblain or predisposition, and, if so, how much cooling is required in these. Smith, Ritchie, and Dawson (1915-16) were prompted by observations upon trench foot, during the last war, to expose the shaved feet of rabbits to damp cold. The rabbits stood on cold or half-frozen mud. Swelling of the feet was visible in forty-eight hours, and subsequently increased ; microscopically they found oedema, perivascular infiltration, and other evidences of vascular damage, including fibrin in the tissue spaces. They thus proved that, in the rabbit, simple prolonged exposure to cold can produce a subacute inflammation of the skin and subcutaneous tissues of the feet. And the time required was about two days. The data we possess indicate that "trench foot" usually requires longer exposure or repeated exposures.

It is noteworthy that patients displaying trench foot for the first time give no previous history of trouble with feet or of chilblains (Smith, Ritchie, and Dawson, 1915-16). Though susceptibility no doubt varies, the lesions may be regarded as occurring in normal people. Chilblains appear on the foot and leg of children paralysed by anterior poliomyelitis, but only when disuse has brought the limb to a state of almost persistent coldness for a long period ; here intermittent exposure of weeks or months is responsible.

*The Predisposing Cause of Chilblain*

It has been suggested that chilblains are associated with an altered blood-coagulation time (Wright, 1897) ; but such change is not found with constancy. The only predisposing cause which can be cited because constant, in the case both of chilblain and of erythrocyanosis of the leg, is an almost habitually defective circulation in the limbs ; so that the temperature of the skin often falls close to that of the surrounding air, in circumstances in which a normal limb circulation would preserve a natural warmth. The limbs are cold not only in cold but also in cool surroundings. There are many distinct conditions in which the blood supply to a limb is defective, and in all these chilblains often occur. Thus they are frequent in the limbs in syringomyelia, anterior poliomyelitis, and conditions of coldness from disuse ; they are found in acrocyanosis, in Raynaud's malady, and in thrombo-angiitis, where blood-flow deficiency results variously in spasm of vessel wall or thrombotic obliteration of the vessels (Lewis and Pickering, 1936).

As the examples of trench foot, and of chilblain in anterior poliomyelitis, illustrate, there is reason to believe that adequate and sufficiently prolonged cooling will produce inflammatory states of the skin originally quite normal. It is to be expected that given exposures will produce chilblain more readily in subjects in whom the skin temperature falls most readily. It is to the high vascular tone of the limb vessels, to the readiness with which the temperature of fingers or other part falls to that of its surroundings, and to the long delay in the release of this spastic condition of the vessels after general vasodilatation sets in, that the chilblain subject seems to owe his predisposition to these lesions.

Smith, Ritchie, and Dawson found in their rabbits that strapping the legs intensified the injury due to exposure ; it is recognized that tight footgear increases the frequency of

trench foot ; and in a chilblain subject I have seen chilblains appear only on a strapped foot when both feet had been equally exposed to cold for some hours in a deliberate test. In all these instances the explanation lies in hindrance to blood supply causing greater cooling on exposure.

The indolence of chilblain and of erythrocyanosis, once such lesions are established, is also clearly explicable on this basis of deficient circulation ; and nothing leads more quickly to recovery than the re-establishment of a flow of blood to the affected parts adequate to bring their temperature to and maintain it at normal levels. The essence of treatment lies in establishing natural warmth. The affected parts are to be directly protected from exposure to cold and from mechanical injury ; and relaxation of the limb vessels is to be induced by warming the trunk with extra clothing, by warmer rooms, and, when necessary, by confinement to bed.

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**SOME EFFECTS OF VITAMINS B AND C ON SENILE PATIENTS**

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The literature on the effects of vitamins B and C on the aged is not great.

**Vitamin C in Old Age**

Yavorsky, Almaden, and King (1934) investigated the amount of ascorbic acid in human organs at different ages. They found that with ageing the organs become poorer in this vitamin. For example, the following amounts of ascorbic acid in milligrammes per gramme of organs were recorded:

	Age: 1 to 30 days	11 to 45 years	46 to 77 years
Adrenals	0.581	0.393	0.230
Brain	0.460	—	0.110
Liver	0.149	0.135	0.064
Kidney	0.153	0.098	0.047
Lung	0.126	0.065	0.045
Heart	0.076	0.042	0.021

A similar decrease with ageing occurred in pancreas, spleen, and thymus. Marinesco, Alexianu-Buttu, and Olteanu (1936) estimated the amount of ascorbic acid in the cerebrospinal fluid (in mg. per 100 c.cm. of fluid), and found in children up to 10 years old 2.8 to 2.2 mg., in persons aged 20 to 30 years 1.4 to 1.1 mg., in those aged 50 to 60 years 0.6 to 0.4 mg., and in those over 70 years old 0.3 to 0.2 mg. A low level of vitamin C in the blood, cerebrospinal fluid, or urine of aged people was also recorded by Plaut and Bülow (1935, 1936), Gander and Niederberger (1936), Altmann and Goldhammer (1937), Monauni (1937), Remp, Rosen, Ziegler, and Cameron (1940). The last-named authors, and also Plaut and Bülow, and Gander and Niederberger, were able to increase this low level by oral administration of ascorbic acid, which appears to exclude the possibility that this condition can be caused by decreased

absorption of the vitamin from the intestinal canal of senile persons. A probable cause of the low vitamin level would be deficiency of vitamin C in the diet of old people. For example, Yavorsky, Almaden, and King (1934), Malmberg and Euler (1935), and Wortis, Wortis, and Marsh (1938) observed a sharp decrease of vitamin C levels in adrenals, liver, brain, and kidneys of guinea-pigs fed on a diet deficient in vitamin C. Also, Schroeder (1939) found in human beings on a diet poor in vitamin C only 0.8 mg. of ascorbic acid per 1,000 c.cm. of blood instead of the usual 10 mg. on a normal diet. These experiments, however, were not on aged persons.

The clinical observations of Plaut and Bülow (1935) and Monauni (1937) indicate that the decreased amount of vitamin C in older persons cannot be explained merely by the low content of this vitamin in the diet, because the difference between young and old persons is present even when both groups are receiving the same hospital diet. Plaut and Bülow, and Wortis *et al.*, have therefore suggested that in senile persons there is a decrease in intensity of those metabolic processes in which vitamin C is taking part. In our opinion the administration of extra-large quantities of ascorbic acid very probably compensates this faulty metabolism or deficient absorption, and this explains the increased content of ascorbic acid in the urine of senile patients receiving large amounts of the acid.

Berkenau (1940) found definite hypovitaminosis-C in senile psychoses, and Bersot (1936) in some mental and nervous diseases. Wortis, Wortis, and Marsh recorded a subnormal vitamin C content of the blood and cerebrospinal fluid in alcoholic patients who suffered also from neuritis or psychopathy. They therefore suggest that a nutritional factor may play a part in the production of mental and nervous diseases. Gander and Niederberger found that treatment of senile persons with adequate doses of ascorbic acid was followed in some cases by improvement of the general health, increased vitality, better sleep, disappearance of rheumatic pains, and a favourable effect on pneumonia of senile patients. Schroeder, reviewing the literature of the subject and the results of his own observations, considers 50 mg. of ascorbic acid to be the minimum daily dose for human beings.

### Vitamin B Complex in Old Age

*Greying of Hair.*—Niemes and Wacker (1922), Hartwell (1923), Bakke, Aschehoug, and Zbinden (1930), and Gorter (1934, 1935) recorded greying, bleaching, or yellowing of hair in rats with dark fur on different deficient diets. Gorter claimed that an insufficient amount of copper salts was responsible in his experiments for the depigmentation of the fur, which he was able to prevent or to cure by the administration of copper salts. Since György (1935) was not able to cure the bleaching of the fur of rats on a vitamin-B-deficient diet by supplementing the diet with aneurin, lactoflavin, and Peters's eluate factor, none of these factors could be considered as the anti-greying compound. Morgan, Cook, and Davison (1938), Morgan and Simms (1939, 1940), Morgan (1941), Lunde and Kringstad (1939), and Mohammad, Emerson, Emerson, and Evans (1939) have confirmed that greying of hair develops regularly on vitamin-B-deficient diet, and, in addition, have proved that of all the B complex the "filtrate factor" alone can prevent or cure this pathological condition. At the same time, the experimental results of these authors suggest that very probably the filtrate factor contains two vitamins, one anti-greying proper and the other growth-promoting. Oleson, Elvehjem, and Hart (1939) also came to the conclusion that the anti-greying vitamin is different from all the known B factors.

Morgan and co-workers produced greying of the fur, and cured it with the anti-greying vitamin, in dogs and silver foxes as well as rats. It still remains to prove, however, that in natural ageing deficiency of this vitamin is at least partly responsible for the greying of hair in old age, and not some other cause. For instance, Morgan and Simms (1940) themselves recorded that injections of cortin and thyroid extract can cure, although slowly, the greying of hair in deficient rats. In his latest paper Morgan (1941) stresses the fact that rats on a diet deficient in the filtrate factor show, in addition to greying of the fur, some other signs of ageing—loose wrinkled skin, sparse hair, atrophic adrenals, and finally emaciation with ulceration of the skin.

### Presence of Some Similar Pathological Changes in Vitamin B<sub>1</sub> or Nicotinic Acid Deficiency and in Senility

Williams, Mason, Wilder, and Smith (1940) produced experimental deficiency in 6 normal healthy women for a period of 88 days on a diet sufficient in all vitamins except aneurin (B<sub>1</sub>). Among the symptoms observed by these authors the following features also often occur in senile patients: depressed mental state, weakness, dizziness, easy fatigability, backaches, soreness and atony of muscles, palpitation, dyspnoea on exertion, reduction of the capacity for physical and mental activity, difficulty of concentration and memory, insomnia, headaches, abdominal distension, and roughness of the skin. McLester (1939) and Spies, Hightower, and Hubbard (1940) give an account of "pre-pellagrous prodromal" forms of nicotinic acid deficiency. In the symptoms described it is also possible to note some features usually occurring in aged people: rashes, symmetrically and bilaterally developing on the skin; mental disturbances such as apprehension, confusion, disorientation, nervousness and forgetfulness, depression, weariness; and also increased fatigability, headaches, and insomnia. While pointing out the similarity of the features, however, we should like to note that the same pathological conditions might be produced by altogether different causes, and therefore the similarity might suggest only the desirability of investigating the possible significance of B vitamins in the process of senescence.

Some encouragement is afforded by the results obtained by Cleckley, Sydenstricker, and Geeslin (1939), who treated 19 patients with nicotinic acid. Of these, 12 were old, with advanced arteriosclerosis, presenting a clinical picture commonly attributed to arteriosclerotic encephalopathy; 5 showed marked deafness. All of them were suffering from hebétude amounting to profound stupor, which was a most prominent feature of the disease. Improvement obtained after the treatment was so remarkable that the authors conclude that "nicotinic acid was life-saving in all but one or two of the cases under discussion." The deafness was also much relieved, especially in two cases.

Another reason for investigating the effects of vitamins B complex and C on senile persons is based on the admission, accepted by most specialists in nutrition, that at the present time a partial deficiency of vitamins B and C is more widely prevalent among the populations of Europe and America than was previously thought. Corroboration of this, for example, is given by the deficiency of vitamin C, referred to above, in the blood, cerebrospinal fluid, organs, and urine of aged people.

### Present Investigation

The total number of patients concerned in the clinical trial at the Littlemore Hospital was 58 (one patient left the hospital after Period III). The effects of vitamins B and C were studied on 40 patients (15 males and 25 females), while the remaining 18 (males) formed a control group receiving dummy pellets of lactic sugar. The investigation was of about a year's duration.

Vitamin B complex was given in the form of dried yeast specially prepared in the Government's Chemical Research Laboratory at Teddington, to the Director of which, Dr. G. S. Whitby, and to Dr. A. C. Thaysen, who was responsible for its preparation, we express our gratitude. The single dose was about 25 grammes, given as a sweetened suspension in water three times a week. The yeast was supplemented by tablets of pure crystalline vitamins, given three times a week in the following single doses: 5 or 3.3 mg. aneurin (B<sub>1</sub>), 5 or 3.3 mg. lactoflavin, and 50 or 33.3 mg. nicotinic acid. We are most grateful to Prof. R. A. Peters, who suggested these doses. Vitamin C was given as pure ascorbic acid three times a week, each dose 200 or 300 mg. All crystalline vitamins B and C were supplied in generous amount by Messrs. Roche Products Ltd., to whom, and in particular to Dr. F. Bergel, we offer our thanks.

Observations on the 40 patients of the experimental groups were divided into five periods, each of 8 or 9 weeks' duration, during which examinations and tests were

repeatedly performed. These treatment periods alternated with rest periods of 10 to 14 days :

*Period I* ("Pre-treatment period").—All patients.

*Period II*.—During this period vitamin B complex preparations were given to 20 patients (first group, 7 males and 13 females), and vitamin C to the remaining 20 (second group, 8 males and 12 females).

*Period III*.—The first group was now given vitamin C, and the second group vitamin B complex. Thus each of the 40 patients was receiving either vitamin B ("Vit. B Groups") or C ("Vit. C Groups") treatment. In the tables (p. 842) the results obtained from groups similarly treated have been pooled.

*Period IV*.—To all the patients of the experimental groups both vitamins B and C were given simultaneously ("Vits. B + C Group") in the doses described above.

*Period V*.—"Post-treatment period" of 4 to 5 months, during which no treatment was given.

In the clinical investigation special attention was paid to changes in senile features (see later). In addition, blood examinations were made on the number of red cells and haemoglobin content. The urine was examined for albumin, casts, and sugar.

Dr. Stephenson applied psychological tests of psychomotor speed (tapping on three keys arranged in triangle fashion) and of psychomotor co-ordination (tapping with two hands co-ordinately on three keys). Besides this he tested (a) muscular power by dynamometer grip for each hand alternately, using the apparatus of Cheron and Verdin; (b) compression power for left arm; and (c) extension power for right arm, using apparatus devised and constructed by him, which will be described in detail elsewhere, together with the results of some additional psychological tests used (reaction to visual stimulus, card-sorting, and manual dexterity).

For economy of space we have tabulated only some of the clinical, psychological, and ergographic results, presenting them in the briefest possible way. Senile features not included in the tables will be discussed in the text.

#### Age and Condition of Patients

The average age of the patients in the treated group was 73, varying from 65 to 86; in the control group 71½, varying from 60 to 87. So far as was possible the patients were distributed evenly in the different groups according to their age and the severity of the senile changes, although these changes were on the average slightly fewer and less severe in the control group.

All the patients were suffering from dementia senilis, which, however, varied greatly in degree; in some cases the dementia was secondary to a previous psychosis. Delusions complicated 13 cases and hallucinations 5 cases. Besides dementia senilis, some or all of the following usual features of senility or those that accompany ageing were present, and their changes were recorded during repeated examinations: increased bony prominences of the face, sunken eyes and cheeks, stooping, general weakness, flabby muscles, uncertain movements, tremors, stiffness of joints and of stretching and bending movements, shuffling gait, rheumatism, flabby shrunken genitalia, obliterated interosseous spaces, parchment skin, wrinkles, rashes, senile itchings, discoloration and pigmentation of skin, senile hair, dry mouth, fissured coated tongue, impaired digestion, constipation, flatulence, husky cracked voice, uncertain slow speech, shortness of breath, dim vision, arcus senilis, red conjunctivae, deafness, arteriosclerosis, varicose veins, haemorrhoids, oedematous eye sacs and ankles, weakened or lost control of bladder and bowel action, dullness of sensory nerve endings, easy chilling, daytime sleeping, and nocturnal insomnia. The number of patients showing some of these senile features is given in Tables I and II, column 2.

Those features in which no numerous or pronounced changes were noted have not been tabulated, but will be mentioned in the text.

#### Excretion of Vitamin B<sub>1</sub> in Urine

The patients received the usual hospital diet, sufficient in calories but restricted in greens (three times a week), fruit, or fresh lettuce (once a week, if available). The vitamin content of the diet was limited. The amount of vitamin C in the organs and urine of aged people has already been repeatedly investigated by other workers, so it was decided to assay the amount of vitamin B<sub>1</sub> in the urine. Every effort was made to collect the whole of the twenty-four hours' urine and to mix it with preservatives (HCl and toluol) as quickly as possible after excretion. This was not easy to arrange with demented senile patients. Therefore, although the qualitative changes obtained in the different groups were clearly defined, the actual figures should be considered with some reservation. The assay of vitamin B<sub>1</sub> in the urine was performed by Dr. H. W. Kinnersley in Prof. R. A. Peters's Department of Biochemistry at Oxford University. We are most grateful both to Dr. Kinnersley and to Prof. Peters for their kind help.

In the urine of the control senile patients not treated with vitamins (16 patients were examined) an average of about 5 γ of vitamin B<sub>1</sub> was excreted during twenty-four hours; in the urine of those treated with vitamin C (9 patients) about 6 γ, and in that of those treated with vitamin B complex (8 patients) 156 γ. The average excretion of vitamin B<sub>1</sub> in the urine of 25 young soldiers suffering from different mental diseases, in the same hospital, was about 34 γ, but their diet contained a little more of cooked and fresh vegetables. Therefore, without further investigations it is impossible to decide whether the very low figures of B<sub>1</sub> excreted in the urine of senile persons were due only, as is the case with vitamin C, to some disturbance in senile metabolism in which vitamin B is involved, or not. The average amount of urine excreted and collected in twenty-four hours was 1,335 c.cm. in control senile persons, 1,006 c.cm. in senile patients treated with vitamin C, 1,556 c.cm. in patients treated with vitamin B complex, and 1,667 c.cm. in the control young patients.

*Body Weight and Fat Deposition*.—Towards the end of the experiment there was a slight loss of body weight in both the control and treated groups, but no pronounced changes were observable in the subcutaneous fat of the patients.

#### Mental Condition

1. *Clinical Observations*.—In most cases the changes in mental condition were not great, but were quite definite. Where, for instance, "improvement" is recorded it consisted in a marked improvement or sometimes even in the disappearance of two or more, or all, of the following abnormalities: the patients became less incoherent and more intelligent in their talk, less depressed or less excited, less restless with fewer aimless movements, brighter and more friendly and sociable and less quarrelsome, and cleaner in their habits; they started to recognize relatives and nurses, performed better work; and nocturnal insomnia and day sleeping improved or disappeared. The percentage of improved cases was much greater and that of deteriorated cases considerably less in the treated (Table I) than in the control groups (Table II), and the number of improved cases grew steadily during the three successive periods of the treatment. After the treatment, although the change for the better was maintained in most of the improved cases, the number of deteriorated cases increased, including some of those which improved during the treatment. The improvement in a few of the treated cases was really remarkable. For example, in one case the patient before

TABLE I.—Effect of Vitamin Treatment on Senile Features of 40 Patients

Senile Features	Pre-treatment Period	Number of Patients with Senile Features during											
		Vitamin B Periods			Vitamin C Periods			Vitamins B + C Period			Post-treatment Period		
		Improvement Occurred	Deterioration Occurred	No Change	Improvement Occurred or Maintained	Deterioration Occurred or Maintained	No Change	Improvement Occurred or Maintained	Deterioration Occurred or Maintained	No Change	Improvement Occurred or Maintained	Deterioration Occurred or Maintained	No Change
Impaired mental condition	40	8	2	30	13	3	24	25	3	11	20	13	4
Stooping	38	12	3	23	9	4	25	21	2	14	6	19	12
Shuffling gait	25	13	0	12	16	0	9	19	0	5	10	8	5
Uncertain movements	22	12	1	9	12	1	9	17	0	4	13	10	2
Tremor in hands	22	10	2	12	6	3	14	19	0	4	4	19	3
Stiff joints and movements	25	11	3	14	10	0	15	20	2	6	6	18	3
Shortness of breath	23	7	3	14	8	1	15	9	4	13	2	12	12
Oedematous ankles	17	8	2	7	7	5	9	13	4	6	5	13	6
Oedematous eye sacs	30	20	1	9	21	1	10	25	2	5	6	22	5
Easy chilling	27	7	3	18	3	7	17	13	4	12	7	12	12
Skin rashes	13	8	1	5	6	0	7	10	2	5	5	9	3
Senile itchings	9	5	2	4	6	0	4	8	3	2	4	10	1
Insomnia	17	10	4	3	12	2	3	14	1	1	6	11	1
Constipation	14	6	1	8	10	0	4	11	0	3	5	13	2
Total No.	322	137	28	168	139	27	165	224	27	91	99	189	71
Change in total No. of features as compared with pre-treatment period	—	43%	9%	52%	43%	8%	51%	70%	8%	28%	31%	59%	22%

TABLE II.—Changes in Senile Features of Patients of the Control Group examined before Administration of "Dummy" Tablets (Examination I) and 5 Months (Examination II) and 9 Months (Examination III) Later

Senile Features	Examination I	Number of Patients with Senile Features					
		Examination II			Examination III		
		Improvement Occurred	Deterioration Occurred	No Change	Improvement Occurred or Maintained	Deterioration Occurred or Maintained	No Change
Impaired mental condition	18	1	5	12	1	7	10
Stooping	16	0	1	16	0	3	14
Shuffling gait	8	1	2	7	1	5	4
Uncertain movements	6	1	0	5	1	2	5
Tremor in hands	12	0	1	12	0	5	10
Stiff joints and movements	11	0	0	11	0	4	9
Shortness of breath	6	0	1	6	0	4	6
Oedematous ankles	1	0	3	0	1	2	2
Oedematous eye sacs	15	3	1	12	3	4	10
Easy chilling	8	0	0	8	1	2	7
Skin rashes and itchings	5	2	1	3	0	10	2
Insomnia	3	0	0	3	0	3	3
Constipation	1	0	0	1	0	2	1
Total No.	110	8	15	96	8	53	83
Change in total No. of features as compared with Examination I	—	7%	14%	87%	7%	48%	75%

the treatment had no control over her bladder and bowel, was dirty in her habits, very depressed and stuporous, showed no intelligence in her behaviour and talk, and did not recognize her relatives or the nursing staff. At the end of the treatment all these abnormalities had disappeared, except for occasional slight confusion in thought.

In the control group delusions were present in 6 patients and hallucinations in 2, and no improvement was recorded in any; in the treated group, in 5 out of 13 cases of delusion a pronounced improvement (in one case disappearance) was noted, and in 1 out of 5 cases there was a disappearance of hallucinations. It should be mentioned, however, that in the "post-treatment period" delusions returned in 4 patients—i.e., in the majority of cases the improvement lasted only during the period of treatment with vitamins. Nocturnal insomnia definitely improved or disappeared in a considerable number of cases (compare Tables I and II), while day sleeping was recorded less frequently in those who were subject to it.

2. Psychological Effects (W. Stephenson).—The objective results of the psychological tests (Table III, Tests 1 and 2)

again corroborated the clinical observations and recorded a definite improvement in the mental condition of the treated group. The results of the psychomotor co-ordination test are perhaps particularly demonstrative, showing as they do some improvement, in a lesser degree, even in the post-treatment period.

TABLE III.—Averaged Effects of Vitamin Treatment as shown by Psychological Tests and those of Muscular Power, compared with the Same Tests (performed at Approximately Two-months Intervals) on Control Senile Persons

Tests	Periods of Observation on Controls :				
	I	II	III	IV	V
	Periods of Observation on Treated Group :				
	Pre-treatment	Vit. B	Vit. C	Vits. B + C	Post-treatment
1. Psychomotor speed :					
Control	100	100	101	105	99
Treated	100	109	113	110	103
2. Psychomotor co-ordination :					
Control	100	102	102	106	102
Treated	100	114	121	119	116
3. Dynamometer grip :					
Control	100	99	105	99	105
Treated	100	110	112	110	103
4. Averaged compression (left arm) and extension (right arm) power :					
Control	100	101	100	99	109
Treated	100	128	122	147	130

Note : The quantitative changes of the tests are expressed as percentages of initial score (taken as 100) of Period I in control senile persons; or, in the treated senile patients, as percentages of the pre-treatment period (also taken as 100).

Muscular System

1. Clinical Observations.—Muscular function definitely improved under the treatment (Table I) as judged by the favourable effects on stooping, shuffling gait, uncertain movements, tremor in the hands, and stiff movements. At the end of the "Vits. B + C period" of the treatment improvement was such in the patients with mild or medium changes that these senile features completely disappeared or were present only in very slight degree—in the case of stooping in about one-quarter, uncertain movement in about three-quarters, shuffling gait, tremors, and stiffness of movement in about a half of all the "improved" cases shown in Table I. Hirata and Suzuki (1935) observed hypovitaminosis-C in patients suffering from progressive muscular atrophy. Treatment with vitamin C improved their condition considerably.

2. Tests with Dynamometer and Ergographs (W. Stephenson).—These tests corroborated the clinical observations and are particularly useful because their results can be

presented quantitatively. As the data for Tests 3 and 4 show (Table III), a distinct improvement was obtained during the treatment with vitamins B and C (the larger differences between the treated and control groups are statistically significant, as will be shown in a later, more detailed, paper on these tests). Ergographic results on arms (Test 4) were much more demonstrative than those with the dynamometer (hand grip, Test 3): this is most probably due to the greater sensitivity, greater reliability, and more comprehensive nature of the ergographic tests as compared with the less reliable and cruder dynamometer.

### Cardiovascular System

There is a convincing amount of literature demonstrating a causative association between cardiovascular disturbances and partial deficiency of vitamin B<sub>1</sub>. These symptoms are promptly cured by vitamin B<sub>1</sub> administration. The extreme form—"cardiac beriberi"—is very dangerous, but even the milder forms call for the closest medical attention. A good summary of the literature on the subject, with an account of their own cases, is given by Weiss and Wilkins (1936) and Weiss (1940). Weiss and Wilkins described these mild forms as various combinations of tachycardia, or vagus reflex irritability with bradycardia, sometimes with asystole and syncope, one-sided heart failure, peripheral arteriolar dilatation or vascular constriction, or vasomotor collapse. Histological changes were found to be similar to those described in "beriberi heart."

In our patients we have not noticed well-defined symptoms as described above. In two, however, *extrasystoles* which had been present for a long time before the treatment disappeared after the administration of vitamin B complex.

No constant or significant changes were observed in the "resting" *blood pressure* and *pulse rate*. Although varying in individual cases, the average figures obtained in all of the 40 patients were remarkably close. For example, the average systolic - diastolic pressure before the treatment was 170/95; at the end of each of the three succeeding periods of treatment the values were 169/86, 169/91, and 167/89 respectively. In the control group the average figures at the beginning and end of the observations were 165/89 and 154/82 respectively. No change was noticed in the degree of *arteriosclerosis* of the treated patients. Some definite improvement was indirectly recorded, however, in the function of the cardiovascular system, because the *shortness of breath* and *oedematous eye sacs and ankles* completely disappeared or were much improved in a large percentage of the cases, as shown by a comparison of the data in Tables I and II. No changes were noted in the condition of the *varicose veins* or *haemorrhoids* of our patients, in none of whom were these conditions severe. Krieg (1938) and Ochsner and Smith (1940) were able to decrease pain in the varicose veins and ulcers considerably, and Krieg even noticed a contraction of the varicose veins after administration of vitamin B<sub>1</sub>. This latter, however, was not confirmed by Ochsner and Smith.

### Skin and Hair

Dullness of the nerve endings in the skin was recorded in 28 of the treated patients; it improved in 9 cases, appeared in one new patient not previously suffering from it, and persisted unchanged in the remaining patients towards the end of "B + C period." In the control group no improvement was noticed in any of the patients; it persisted in 12 who had had it from the beginning, and newly appeared in 2 others. Complexion, wrinkles, and parchment-like skin were also unchanged, but the senile patchy pigmentation of the hands appeared to be less pronounced in most patients at the end of the third period of

the treatment. Quite definite improvement or in some cases complete disappearance of senile skin itchings and rashes was recorded (Table I) in a considerable percentage of the treated cases, the highest figures being obtained when vitamins B and C were administered simultaneously. In the control group (Table II, Examination III) no such improvement was recorded.

In the literature some favourable results were recorded with vitamin B in skin diseases; for instance, pellagra rashes could be quickly improved by the administration of nicotinic acid and aneurin (Boyd Campbell and Allison, 1940). A good result was obtained by Kristensen and Vendel (1940) in the treatment of chronic eczemas with yeast extract, and by Madden (1940) in the case of psoriasis treated with aneurin.

No changes were noticed in the grey hair, growth of bristles, or baldness in the treated senile patients. The scarcity or absence of hair in the axilla was also un-influenced.

### Digestive Tract

The tongue was fissured or coated, or both, in 22 cases; by the end of the third period of treatment it became better or normal in about half of them, while dry mouth disappeared in only a few. Constipation was a symptom which improved or disappeared in most of the treated patients (Table I) but in none of the controls (Table II). The treatment had no effect on flatulence. No other serious disorders in gastro-intestinal function were noted. Satisfactory results in the treatment of cases of constipation with aneurin have repeatedly been published, and a good review of the literature on the subject has been given by Harris (1938). Gastro-intestinal distension and atonia have been found to be prominent features of aneurin deficiency both in men and in animals (Harris, 1938).

### Other Senile Features Examined

Easy chilling improved or disappeared after combined treatment with vitamins B and C in about half of those cases in which this feature was present before the treatment (Table I); the body temperature did not on the average show any definite changes in all the five periods examined. Husky cracked voice, present in different degree in almost all the treated and control patients, became clearer in only 2 of the treated cases.

Uncertain slow speech persisted in 3 patients and appeared in 3 more of the control group at the end of the period of observation. In the treated group it was present before treatment in 11 patients, in 5 of whom it definitely improved or disappeared; but 2, not affected in this way before the treatment, had begun to suffer from it by the end of the third period.

Rheumatism, atrophied interosseous spaces, deafness, dim vision, arcus senilis, and red conjunctivae were not definitely changed in either the treated or the control group.

### Red Blood Cells and Haemoglobin

Although varying in individual cases, there was on the average in the treated group a hardly significant increase of the red cells and haemoglobin during the treatment. (The respective figures were: before treatment—red cells 4,850,000, Hb 89; vitamin B groups, 5,090,000 and 92; vitamin C groups, 5,160,000 and 99; vitamin B + C groups, 5,110,000 and 93.) In the control group the decrease of red cells from 5,080,000 to 4,930,000 and of Hb from 93 to 89 was also insignificant.

### Post-treatment Period

If the data of the "post-treatment period" (Table I) are compared with those of the previous periods in the experimental group and with those of the last examination

in the control group (Table II), it becomes clear that certain typical changes occurred after the end of the treatment. Thus about four months after the treatment finished considerable deterioration had occurred, consisting in particular of disappearance of the improvement obtained during the treatment, and also of the appearance of some new cases of deterioration. This indicates that in some cases improvement of certain senile features and prevention of further senile deterioration can be maintained only if treatment with the vitamins is continued. In spite of this relapse in a number of cases, however, in numerous others the improvement obtained by the vitamin treatment was maintained after its discontinuation. This was demonstrated by the clinical observations (Table I), the psychological test (Table III, Test No. 2), and the ergographic test (Table III, Test No. 4).

Experiments on deficient animals have shown that the specific effects of vitamins B and C do not last long after the end of the administration of these vitamins. Therefore it is most probable that the explanation of the lasting action of the vitamins in some of the senile patients lies in the disruption of those secondary vicious circles which are originated by pathological changes in different organs (e.g., sex glands, adrenals, gastro-intestinal canal, liver, etc.), changes in these organs in their turn being produced by the direct action of vitamin deficiency. These secondary pathological conditions, being specific for dysfunction of the affected organs, become additional to those caused by pure vitamin deficiency proper. Of course, when the effects of the discontinued vitamin treatment have worn off, the repair of the organ concerned disappears after some time and the secondary vicious circles return.

### Summary

Forty senile patients were treated with vitamins B complex and C, the whole period of observation lasting for about a year. The condition of these patients was compared with that of 18 senile patients of a control group receiving dummy tablets. All patients were on a usual hospital diet not rich in vitamins.

Treatment with vitamins B and C, as with any other remedy, did not stop the biologically inevitable development of senility, and therefore did not affect those basic features which are specific for and present in even the most physiological type of senility.

By treating the aged people with vitamins, however, it was possible to prevent or improve, in some cases to a striking degree, certain of those senile features which could be considered as pathological, because they appear prematurely or in an extreme degree (e.g., muscular, cardiovascular, and mental deterioration) or which do not seem to be inevitable in normal physiological senility (e.g., dementia, insomnia, skin rashes and itchings, constipation).

During the period of observation improvement or disappearance (apparently not of a lasting nature) of some pathological senile features was observed in numerous cases, while a number of other cases were not improved by the treatment, and a few patients who had been free from certain senile features developed them during and notwithstanding the treatment.

In spite of the comparatively limited and modest results which aged people might expect from treatment with vitamins, it seems clear that in suitable cases the relief obtained in some pathological senile features might be considerable.

The results obtained provide strong support to the argument, repeatedly emphasized by several specialists in the modern science of nutrition, that the greatest care should be taken to prevent the occurrence of partial or latent vitamin deficiency, apparently widely spread in the population. This will result not only in the prevention of certain vitamin-deficiency diseases but probably also in the approach to a less pathological senility.

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## THE VALUE OF BLOOD TRANSFUSION IN MALIGNANT DIPHThERIA

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Judging by the lack of any published reports in English medical literature on the value of blood transfusion in malignant diphtheria, it would seem that this method of therapy has received little or no attention in this country. On the other hand, a review of the available literature goes to show that the subject has engaged the attention of certain Continental workers for some time.

Baar and Benedict (1933) treated 43 cases of malignant diphtheria with either "human serum" or blood transfusion. All the cases selected for treatment by transfusion were rigorously classified, nor were desperate cases with cardiac insufficiency discarded. Twenty-seven of the 43 cases recovered, giving a case mortality of 37.2%. The authors claimed that transfusion reduced the mortality rate of malignant diphtheria by one-half.

Moeller (1934) tried the method of giving blood in the proportion of 1/70 of the patient's weight. In all he transfused 19 cases: 5 were transfused late in the illness (6th, 7th, or 8th day), and of these four died; 2 were moribund on admission and died; of the remaining 12 cases, 7 survived. Moeller calculated the mortality rate at 41% in the transfused cases and at 66% in the non-transfused, but intimated that the number of cases was too small for any firm conclusions.

Darrow and Yannet (1935) emphasized the value of blood transfusion in malignant cases as a method of combating the