are taken in the form in which Nature provides them in well-balanced combinations of unsophisticated food materials. Some individuals appear to require more vitamins than others, size being an important factor in determining their requirements; some species of animals require more of a particular kind of vitamin than others; more are needed for reproduction than for growth, and more for optimum well-being than for the prevention of the named deficiency diseases; more are required by the lactating than by the non-lactating animal, and more for longevity than for a shorter life. The amount needed varies with the composition of the food, with its balance in other essentials, and with its digestibility; more of one vitamin is required when the food is very rich in another—as, for instance, more vitamin C when the food is rich in vitamin D; there is for optimum nutrition an ordered balance even amongst the vitamins themselves. In short, the amount of vitamins needed varies with the metabolic requirements of the individual; the attainment and maintenance of physical perfection, heavy work, reproduction, lactation, digestion, exposure to cold, infectious and debilitating diseases, are all indications for their liberal supply.

Before bringing this brief survey to an end I will refer to another aspect of the matter: the effect of vitamin deficiency in increasing the susceptibility to certain poisons, which the work of Smith, McClosky, and Hendrick has recently brought into prominence. Deficiency of vitamin A increases the susceptibility of mice to *botulinus* toxin, and also their susceptibility to mercuric chloride. Deficiency of the same vitamin induces in rats an enormously increased susceptibility to morphine, to ergotoxine, and, in lesser degree, to histamine. Deficiency of vitamin B like-

wise increases greatly the susceptibility of rats to ergotoxine and to pilocarpine. Stimulants of the central nervous system are all more toxic to rats receiving too little vitamin A than to well-fed animals.

Observations of this kind suggest that the ability of the tissues to detoxify certain poisons—both bacterial and other—is reduced by diets deficient in vitamins; while indicating that such diets increase the sensitivity of the nervous system and of its autonomic division to toxic agents. Not only may this be so, but the disturbances of metabolism which result from vitamin insufficiency may themselves give rise to toxic metabolites which exercise specific effects on certain organs and tissues of the body. This I believe to be the case in beri-beri. Most of us will probably agree that there is such a thing as a specific beri-beri-producing poison, though disagreeing as to whether it be produced in rice before this food is ingested, or in the intestine by some bacterial agent introduced with rice, or in the course of a disordered metabolism arising out of vitamin insufficiency. Our disagreements will not greatly matter so long as we recognize the prime importance of a sufficiency of the antineuritic fraction of vitamin B in preventing beri-beri.

The newer knowledge of nutrition is, I am convinced, the greatest advance in medical science since the days of Lister. When physicians, medical officers of health, and the lay public learn to apply the principles which this newer knowledge has to impart, when they know what malnutrition means, when they look upon it as they now look upon sepsis, and learn to avoid the one as much as they now avoid the other, then will this knowledge do for medicine what asepsis has done for surgery.

PERNICIOUS ANAEMIA TREATED WITH LIVER DIET.

BY

F. A. PHILLIPPS, M.D., B.Ch. Cantab.

THE following case appears to be of some interest in view of the severity of the symptoms, the age of the patient, and the rapidity of the improvement with liver diet after a prolonged course of arsenic had failed to produce appreciable alteration in the blood count.

A widow, aged 68, had had no severe illness, though always delicate. She had undergone hysterectomy (with ? double ovariectomy) at the age of 35, and had taken $1\frac{1}{2}$ grains of thyroid extract daily for fourteen years for myxoedema. Her husband died three years ago; she had a "nervous breakdown" two years later, and was put on tablets of iron, arsenic, and strychnine for anaemia; these she took on and off until January, 1926.

In July, 1926, numbness and tingling of both feet with oedema occurred, and gradually extended up the legs. In January, 1927, she presented a very definite yellow tinge, complained of morning nausea, severe yellow-coloured diarrhoea, weakness, and breathlessness. The lips and mucous membranes were pale.

A blood count done by the Laboratories of Pathology and Public Health on November 12th, 1926, was as follows:

Red cells ...	1,670,000	Small mononuclears ...	39 per cent.
White cells ...	7,000	Polymorphonuclears ...	53 "
Haemoglobin ...	45 per cent.	Large mononuclears ...	6 "
Colour index ...	1.36	Eosinophils ...	2 "

Poikilocytosis markedly present.
Anisocytosis and polychromasia present.

The blood pressure was 162/62. The heart and lungs were normal, the reflexes slightly exaggerated. There were no retinal haemorrhages. The urine was normal in colour and contained no albumin or sugar.

The removal, in January, 1927, of septic lower incisor teeth and a septic molar was followed by temporary improvement in her clinical condition. In April she had an attack of cystitis which necessitated treatment for ten days.

From May to September, 1927, she was taking arsenious acid tablets (gr. 1/20 twice daily after food), but although the clinical condition had improved somewhat, a blood count done on September 10th by the same pathologists showed no improvement.

Red cells ...	1,670,000	Small mononuclears ...	43 per cent.
White cells ...	2,500	Large mononuclears ...	5 "
Haemoglobin ...	45 per cent.	Polymorphs ...	50 "
Colour index ...	1.30	Eosinophils ...	1 "
		Mast cells ...	1 "

The red cells showed moderate variations in size, large average size; there was moderate poikilocytosis, slight polychromasia, and no abnormal white cells.

She was first seen by me on September 20th, 1927, and was then very yellow, weak, and breathless on exertion; she complained of palpitation, sore tongue, eructations after food, and tingling and numbness of the feet. The tongue was "beefy," dark red, and tender, the lips and mucous membranes pallid. There was a slight systolic murmur at the apex. There was no oedema of the feet, but cutaneous anaesthesia, both epicritic and protopathic, of both feet and legs up to the thigh. Heat and cold were well appreciated. The knee-jerks and ankle-jerks were normal, the plantar reflexes flexor; the skin over the feet was dry and atrophic. Vibration was appreciated in the tibiae.

A blood count by Dr. J. Bamforth of St. Thomas's Hospital, on October 11th, was as follows:

Total red cells ...	1,910,000	Polymorphs ...	38 per cent.
Total leucocytes ...	2,080	Small lymphocytes ...	44 "
Haemoglobin ...	42 per cent.	Large lymphocytes ...	8 "
Colour index ...	1.1	Eosinophils ...	2 "
		Large hyalines ...	7 "

There was much poikilocytosis and anisocytosis. Punctate basophilia was present; megaloblasts found. The blood count corresponded in all particulars with that of a true pernicious anaemia.

For a fortnight before the taking of this blood count the patient had been so weak and ill, and complained so bitterly of persistent diarrhoea, that the arsenic had been suspended and she was having only dilute hydrochloric acid (m xv thrice daily). She was then extremely weak and ill, and was only capable of leaving a sofa for meals, which was a necessity.

On October 11th a diet containing 7 oz. of calf's liver per diem was given, partly as raw sieved pulp and partly as cooked liver. The raw liver (4 oz. sieved weight) was given mixed with half a cupful of orange juice with water added, and taken at 11 a.m.; the cooked (3½ oz. fried) liver was taken as the evening meal with a rash of bacon. Fresh fruit and vegetables were recommended and fats other than the bacon and butter were forbidden. Ostelin tablets (one thrice daily after food) were prescribed, the rest of the diet being to taste. At the end of a fortnight from the commencement of treatment improvement became evident. The lips were redder and the yellow tint paled. She was then able to walk freely about the room. Diarrhoea ceased, and she has since continued to improve. The cheeks are now no longer pallid.

On November 22nd a further blood count by Dr. Bamforth gave the following result:

Total red cells ...	5,580,000	Polymorphs ...	68 per cent.
Total leucocytes ...	7,200	Small lymphocytes ...	17 "
Haemoglobin ...	72 per cent.	Large lymphocytes ...	2 "
Colour index ...	0.65	Large hyalines ...	4 "
		Eosinophils ...	8 "
		Mast cells ...	1 "

No poikilocytosis or anisocytosis.

At present (December 2nd, 1927) the patient is apparently in good health, though thin; her appetite is not good, the lips and mucous membranes are no longer pale, the lemon tint has almost entirely disappeared.

She still complains of a feeling of breathlessness, but this was a feature of the "nervous breakdown" two years ago. Anaesthesia to pinprick is still present, but is patchy in distribution. Epicritic sensibility appears to show definite improvement. The feet are bluish in colour and the skin is dry and atrophic; numbness, tingling, and coldness of the feet are still complained of, though less so. Knee-jerks and ankle-jerks are present and equal; the plantar reflex is flexor. No retinal haemorrhages can be found.

She is now permitted to replace one portion of the liver with underdone steak or kidneys on three days a week, and, oddly enough, prefers to replace the cooked portion rather than the raw. The raw liver can also be conveniently given in sandwiches or in a jelly, which can be flavoured to taste with bovril, lemon, etc.

It is, of course, too early to make any claim to permanent effect, but the rapidity of improvement appears to be remarkable in a patient of this age.

My thanks are due to Dr. H. M. McCrea for his kindness in giving me full particulars of the patient's past history and treatment, and to Dr. J. Bamforth for the blood counts.

THE THYROID AND MANGANESE TREATMENT.

A SUGGESTION WITH REGARD TO ITS POSSIBLE MODE OF ACTION.

BY

HERBERT W. NOTT, M.R.C.S., L.R.C.P.,
GUILDFORD.

NEARLY three years have elapsed since this treatment was promulgated; it has been widely and successfully practised, and the time seems to have arrived for a tentative investigation as to its possible mode of action. Some good will have been gained if such an inquiry helps to dispel certain views which are quite misleading. For example, the reports of acute pneumonia being rapidly cured by rectal injections of a solution of potassium permanganate have led some to disagree with the title of the treatment and suggest that the thyroid substance may be unnecessary, the possibility being overlooked that, by using potassium permanganate in the way we do, the thyroid gland may be relieved of its load and be allowed to function normally. Yet this was clearly foreshadowed in a paper in this JOURNAL in 1925 (vol. i, p. 443), where, under the heading of "goitre," the following results of treatment were given.

Parenchymatous Goitre.—Four cases are reported to have quickly responded to the treatment, two of them without the use of thyroid extract. One is inclined to relapse, unless she keeps up the treatment occasionally.

Exophthalmic Goitre.—Three mild cases find themselves very much better, with increased weight, and diminution of symptoms, after a few weeks' to a few months' treatment. Two advanced cases describe themselves as "less nervy," and the swelling of the neck has diminished in size. One case of enlarged thyroid gland is reported as having been on the point of having the operation of thyroidectomy, but shortly after the treatment was used operation became unnecessary. In another very severe case no relief at all was obtained after five weeks' continuous treatment, with injections.

Since then nothing has been more obvious to numerous observers than the satisfactory reduction in the size of goitres, so that, whether the thyroid substance is produced by the individual directly, or whether it is necessary to administer it where greater inefficiency exists, the treatment need not be looked upon as incorrectly named.

Some have loosely ascribed its action to the liberated oxygen, without explaining how this occurs. That it cannot be due entirely to oxygen seems quite certain, or why should we not get similar good results from the use of sodium permanganate?

Basic Principles Underlying Treatment.

In this paper it is suggested that an increase of oxidative processes in the tissues and fluids of the body is produced by the interaction of manganese, potassium, thyroid gland substance, and the liberated oxygen derived from the permanganate on reduction. In support of this hypothesis, the more recently acquired knowledge of the elements comprising the combination will be considered in conjunction with the accepted laws of oxidation. An argu-

ment will be adduced tending to show that a reinforced catalytic action must be set up in the blood and cells of the organism by which firmly established metabolites are expelled, to the relief of the autonomic nervous system and the internal secreting glands.

As biology teaches that life itself depends upon oxidation, so also biochemistry has taught that, when oxidation is incomplete or hampered, disordered function results; and as this is the very core of our subject, oxidation will be considered first.

Oxidation.

Bayliss summarizes oxidation as follows:

"Oxidation in the tissues is due to the presence therein in the first place of an organic substance which is readily oxidizable by molecular oxygen. A part of the energy set free in this process is made use of to form from other molecules of the substance an unstable peroxide. Benzaldehyde undergoing oxidation in air is an instance of such reaction. The analogous substance present in cells corresponds to what was originally called by Bach an 'oxygenase,' because it is by its means that molecular oxygen is activated. This activation is produced by the agency of an enzyme, peroxidase, which is a colloidal hydroxide of iron or manganese, kept active, or protected from precipitation or aggregation, by a stable or hydrophile colloid. This enzyme decomposes the peroxide with the liberation of 'active' oxygen, with its powerful oxidizing properties. We are still in ignorance as to what this form of oxygen is, but there seems to be much evidence to show that electrical forces play an important part."—W. M. Bayliss: *The Nature of Enzyme Action*. Fourth edition, 1919, p. 158.

This quotation reminds us that both manganese and iron must be present in the tissues before complete oxidation processes can take place. Now, if some people are not obtaining a sufficiency of either of these two essentials to oxidation, the fact that the consumption of meat has increased so much among Western peoples in the last few years would suggest that it is not the iron content of the food which is at fault.

Potassium.

Mathews of Chicago, who established the prime importance of potassium in the chemistry of the cell, writes:

"Another substance which is in some way concerned in the respiration of the cell is the element potassium. It has been found that in the presence of potassium hydrate, phloroglucin and similar substances undergo oxidation better than with the equivalent amount of sodium hydrate. This indicates that the potassium salt is more easily oxidized than the sodium. There must be some reason for the preference cells have for potassium over sodium. A general richness of potassium in cells of widely different character indicates that this element must be concerned with some fundamental process or condition in the cell, and it is possible that that process is respiration. But just why it is favourable, or what its real function is, it is impossible to state."—A. P. Mathews: *General Cytology*, Chicago, 1924, p. 55.

This, then, may account for the moderate success with the sodium salt.

Manganese.

Manganese has been shown by Bayliss to be essential to oxidative processes; it is found in the ash of all enzymes, and is a most potent catalytic agent. It increases antibody formation.¹ It is essential to growth, not only to the body generally, but to the thyroid gland.² Manganese exists in deficient quantity in white flour; wholemeal flour is rich in it.³ Artificial enzymes have been produced with alkaline solutions of manganese in gum arabic (Bertrand's "laccase").⁴

For some time it was hard to conceive how manganese entered the blood stream, seeing that it exists after reduction as the insoluble salt Mn_2O_3 . But it has been suggested that it probably forms a laccase with the mucus of the bowel or stomach, taking the place of Bertrand's gum arabic, and enters the blood stream as colloids do.

The Thyroid Gland.

The following appear to be the chief points in the later knowledge of this gland which are applicable to this subject.

1. The thyroid gland is generally considered to be the chief activator of oxidative processes, and is now given pride of place in the control of the endocrine system.

2. It is intimately concerned in regulating growth, and is profoundly affected by insufficiency in the food of growth-promoting factors of all kinds.