POLYAVITAMINOSIS AND ASULPHUROSIS

BY

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H. Strachan (1897) described some cases he considered to be an unrecorded form of neuritis. The first external signs noticed were often redness and irritation of the eyelids and lips, which soon passed into a slightly eczematous condition at the corners of the mouth. Sometimes there was a similar condition in the muco-cutaneous line in the prepuce; more rarely there was the same condition of the vulva and anus. There might be much loss of surface epithelium on the tongue, and dimness of vision was a cause of frequent complaint. H. H. Scott (1918) referred to these cases in his work on an acute outbreak of central neuritis in Jamaica, expressing the opinion that the elucidation of the cause of the former disease would clear up the mystery of the central neuritis.

E. Jenner Wright (1927) described a syndrome which he attributed to a deficiency of vitamins A and B in the diet. At that time, as H. S. Stannus (1930) remarks, he did not distinguish in vitamin B the two factors, anti-neuritic B₁, and anti-pellagra B₂, as demonstrated by Goldberger (1926). However, in an article in a later publication (*Dietetics in Warm Climates*, 1930) the two recognized factors of the vitamin B complex were given consideration, and attention was drawn to the evidence showing that the lesions due to a B₂ deficiency tended to ulcerate whereas the A avitaminosis lesion did not ulcerate but was degenerative with keratinization. It is nevertheless interesting to note that J. L. Rosedale (1935) wrote: "The scientific outlook of vitamin B has changed considerably, although it does not yet seem possible or necessary to differentiate the parts of the complex in practical human dietetics."

Clinical Characteristics

The A and B avitaminosis disease was described as being distinct from pellagra and beri-beri, characterized by lesions of the mucous membranes and skin, especially evident at the muco-cutaneous junctions, associated with or followed by disorders of the nervous system, and curable by the addition of cod-liver oil and yeast to the diet. The early symptoms are glazing of the tongue from loss of filiform papillae with soreness and smarting. The angles of the mouth become sore, the anus, scrotum, or vulva eczematous, the skin often rough and showing a keratosis especially evident on the extensor surface of the forearm nearer the elbow than the wrist, and of the thigh nearer the knee than the hip. The tongue is tremulous. External eye symptoms are shown by a glazed, varnished appearance of the skin at the canthi, irritable and inflamed conjunctiva, and sometimes lachrymation. In other cases the ocular conjunctiva is anaesthetic, and in this connexion it should be noted that R. H. Elliot (1920) refers to decreased sensibility of the cornea and conjunctiva, and also to retrobulbar neuritis, as eye symptoms of beri-beri.

The appearance of the face and tongue are well illustrated in Leitch's *Dietetics in Warm Climates* (1930), and the excellent photographs of monilia dermatitis, as it involves the scrotal region, illustrating a paper on dermal moniliasis among natives of West Africa by E. C. Smith (1930), give an exact pictorial representation of the scrotum in the A and B avitaminosis disease. It is interesting to note that Smith, in his histological findings in moniliasis, states that "hyperkeratosis and parakeratosis are constant findings, and usually dominate the microscopical picture."

J. M. H. MacLeod (1930) notes, when referring to a condition generally known as "perlèche," which is indistinguishable microscopically from the mouth lesion

described in the A and B avitaminosis disease, that the organism found in the lesion is a monilia which may be pathogenic or not. The mucosal and skin affections are considered due to vitamin A deficiency, while tremor of the tongue is regarded as the first evidence of nervous symptoms. There follows a train of symptoms implicating the nervous system—namely, alteration in the knee-jerks, often with asymmetrical reactions, sensations of heat, cold, or of "pins and needles" in the extremities, and dimness of vision shown as day-blindness. There is also increasing difficulty in walking and in using the upper extremities. Epigastric discomfort is a cause of constant complaint.

Synergism of Vitamins A and B

H. S. Stannus (1934), in a letter to the *Lancet*, writes: "Mellanby believes pellagra to be due essentially to a vitamin A deficiency. He [Mellanby] thinks that the nervous lesions found in his experimental animals fed on a vitamin A deficient diet are comparable to those in pellagra, and further holds that the pellagrous eruption is due to the same deficiency; he says 'the pellagrous skin lesions are clearly due to loss of a neurotrophic control.' To meet the objection of those who have followed Goldberger, he suggested that vitamin A may be rendered ineffective 'in the absence of some other nutritional factor such as vitamin B₂.'" These remarks are of particular interest in the light of the clinical results given in this paper, which go to show that vitamins A and B work synergically, and may be ineffective in the absence of sulphur, which is shown to be another nutritional factor.

Patients with the disease not too advanced recover on the administration of cod-liver oil and marmite; but in neglected cases with marked paresis months may elapse before they recover sufficiently to walk about. The failure of vision, which is a common symptom, especially in school children and pregnant women, responds readily to treatment if started in time. It should be recorded that the fat-soluble vitamin concentrates, radiostoleum and advita, are efficient substitutes for cod-liver oil; essogen, which is vitamin A without D, has not proved quite so effective. There is experimental evidence which shows that ultra-violet irradiation causes an increase in the sulphur content of the blood. Unfermented palm juice is a useful substitute for yeast.

During many years of observation and treatment of these cases it has become abundantly evident that the most rapid cures with vitamin therapy alone are obtained when vitamin B is used in conjunction with vitamin A. M. McDowall (1930), writing of the A and B avitaminosis disease, states: "Mild cases respond to prolonged treatment with large doses of cod-liver oil; the most rapid cures are effected with cod-liver oil and fresh unfermented palm juice." Palm juice is a rich source of vitamin B even when unfermented. This is important because it has been suggested that the large sulphur content of yeast is responsible for the curative properties of yeast in pellagra.

At this juncture the observation of G. W. Bray (1928), on the synergic action of vitamin A and vitamin B, may be recalled. He reports: "Vitamin A is the chemical impulse which hastens or regulates growth. In its presence cellular multiplication takes place, and in supplying the necessary impulse it is itself oxidized. Vitamin B is the chemical impulse regulating function; it hastens the rate of renewal of energy, and thus enables the cell to fulfil its offices efficiently. In favour of the synergic action of the growth-promoting and function-fulfilling vitamins, there is abundant evidence both experimental and practical." In the experimental evidence Bray draws attention to the ability of vitamin B to counteract the bad effects of an excess or deficiency of vitamin A, inasmuch as the addition

of B allows the absorption and utilization of A, and furthermore permits the utilization of any reserves of A that may have been on hand when B ran out.

Since the description of the symptom-complex under the designation A and B avitaminosis disease, a good deal of attention has been focused on it, and it has been reported as prevalent in various parts of the world. In the Seychelles, by J. T. Bradley (1928) a disease called "decoquée" was described as being prevalent on the outlying islands, corresponding closely with the Sierra Leone disease.

In Nigeria, Moore (1934) described the epithelial lesions of the same syndrome, while paying particular attention to the defective vision which he attributed to retrobulbar neuritis. He does not describe any of the other recorded nervous manifestations, but considers that the syndrome offers for research a means of linking together other deficiency diseases, such as pellagra and beri-beri. This suggestion is of particular interest in view of the fact that one of the eye symptoms of beri-beri is retrobulbar neuritis.

R. H. Elliot (1920) states that in 1895 Kono published six cases of beri-beri, associated with amblyopia, central scotoma, and contraction of the visual field, but presenting no fundus changes. Three years later Komoto discovered that the cause of the amblyopia and of the central scotoma was to be sought in a retrobulbar neuritis. Yamamoto seems to have been the first (1903) to draw attention to an atrophic condition of the temporal disk in these cases. Kagoshima, in 1918, made an anatomical examination of five cases in which beri-beri scotoma was present; he found in all of them a distinct and limited atrophy of the fibres in the outer section of the optic nerve.

Localization of Early Lesions

Attention should now be drawn to the distribution of the epithelial lesions which are the earliest evidence of the disease—that is, on the tongue, lips, angles of the mouth, scrotum or vulva, and conjunctiva. The significant fact emerges that these are the areas richest in certain special cutaneous sense organs, called end-bulbs, which are also found in the sheaths of nerve trunks, synovial membranes, and intestinal mucosa. These end-bulbs are sense organules, composed of modified epithelial cells, in which the delicate terminations of the nerve filaments end.

While considering the distribution of these early lesions, the very common early symptom of failure or dimness of vision—a loss of central acuity of vision—may be discussed. The failure of vision—day-blindness as opposed to night-blindness—is characterized by being most marked in bright light, very little inconvenience being noted at dusk or night time. The rods and cones are the sense organules of the retina and are of epithelial origin. It is generally conceded that the cones are concerned with visual acuity in bright light, and that they are found to be the only element at the centre of the retina—no rods being present—but as the periphery is reached the proportion of rods to cones steadily increases until very few cones are found.

The rods, which are associated with the presence of visual purple, are situated in the regions of the retina, which react to light of low intensity—that is to say, they are concerned with night-blindness. The cones are longer and more highly developed than the rods. They would appear to be the special epithelial sense organule of the retina to suffer in the syndrome of A and B avitaminosis, just as it is possible that the end-bulbs are the special epithelial sense organules to suffer first among the sense organs in the skin and mucous membranes.

The sense of hearing is certainly often affected, but, so far, in cases investigated for loss or alteration in the sense of smell and taste, no impairment has been detected. It must be recorded, however, that the results of subjective

examination in the patients under consideration are not so reliable as they would be if obtained from more educated people.

The non-impairment of the sense of smell may be accounted for by the first cranial nerve differing from all the other sensory nerves in having its nerve endings in direct contact with the air. The apparent non-involvement of the sense of taste may be explained by the origin of the epithelial constituents of the taste buds differing from that of all the other special receptors—the epithelial elements in the taste buds are derived from entoderm whereas all the others are from ectoderm.

All the early symptoms of the disease then are traced primarily to a disturbance in areas containing certain epithelial elements which probably depend on both vitamins A and B for their integrity, efficient working, and functioning. Just as the multiple neuritic lesions are always secondary to the epithelial lesions, it seems reasonable to assume that the evidence of neuritis of the optic nerve, sometimes observed in the disease, is secondary to the retinal lesion in which the cones are involved. Using an Emesay reflexless ophthalmoscope, I have recently examined a large number of cases of defective vision, but I have not found any observable pathological changes in the optic disks in the majority of fairly recent cases associated with epithelial lesions of the disease.

In view of the synergic action of vitamins A and B, coupled with the knowledge that a deficiency of a vitamin in the body may cause a different syndrome under different conditions, there would not appear to be any objection to the acceptance of a vitamin A deficiency in this disease merely on the grounds of the apparent absence of night-blindness from the syndrome. Furthermore, the work of A. Jores (1933), "Concerning the Function of the Pigment Hormone in the Human Organism," shows that the form of pigment hormone known as the melanophore hormone takes part in pigmentations of human beings. In this work it was shown that the melanophore hormone has an influence on the dark adaptation of the human eye. There was an acceleration of about twenty minutes in the adaptation speed when the hormone was dropped into the eye of a person with normal sight. Thus it was shown that the hormone was involved in the formation of visual purple. Intravenous injection also caused acceleration of the speed of dark adaptation, showing that the hormone is probably carried by the blood stream.

It seems reasonable to assume the possibility of the deeply pigmented negro race being naturally endowed with an ability to produce better supplies of the melanophore hormone than the fairer races; there would be, consequently, a decreased liability to night-blindness in the presence of certain degrees of A avitaminosis which would cause night-blindness in persons not so endowed. In Ceylon, L. Nicholls (1934) describes the same deficiency disease and considers it due to vitamin A deficiency only; the Editor of the *Indian Medical Gazette*, however, indicates in a footnote to the paper that there is a vitamin B deficiency in the dietary of the people under discussion.

Therapeutic Experiments

In Malay, Landor and Pallister (1935) describe the syndrome, but ascribe it to a B₂ deficiency. It is significant, in view of what has been written concerning the synergic action of vitamins A and B, that these observers did not intentionally administer the two vitamins together in their experiments in the treatment of the disease. In one experiment they first gave cod-liver oil (2 oz. daily) for four weeks and found no improvement. They then gave the same patients the equivalent of 1 oz. of orange juice daily for three weeks with no improvement, some of the

patients getting worse. They finally gave the same ten patients $\frac{1}{2}$ oz. of marmite daily, when they began to improve rapidly, most of them becoming nearly well in two weeks. Nine of the ten were completely cured after twenty-six days of marmite. No allowance or provision was made in this experiment for the capacity of the body to store vitamin A.

Another ten patients were placed on a daily dose of 4 oz. of yeast—which was estimated to contain 18 grams of dried yeast—considerably more yeast than was given in their previous experiment when $\frac{1}{2}$ oz. of marmite was allowed daily. Nevertheless, the result was not so good, the probable explanation being the absence of the preliminary dosing with vitamin A. In a third experiment, when $\frac{1}{2}$ lb. of liver was given daily, they got most rapid cures. They stated that the immediate improvement with liver was greater than with yeast or marmite; this is as would be expected, for they were giving a rich source of both vitamins A and B.

It should here be observed that no note of a vitamin A concentrate being used in these experiments is recorded. In Sierra Leone we have found sometimes that cod-liver oil does not appear potent and at other times cannot be absorbed. In these cases the vitamin A concentrate should be used by the parenteral route before deciding against its efficacy in disease.

Concluding this introductory portion, in view of the efficacy of sulphur in the cure of the syndrome, as will be shown presently, it should be recalled that there is evidence that the A and B avitaminosis disease can be cured by the administration of vitamin B in the form of fresh palm juice and vitamin A as a concentrate. Consequently, their deficiency must remain an important aetiological factor in the disease, especially in view of the frequent precipitation of the disease by pregnancy. Although this condition possibly causes desulphurosis, it undoubtedly causes devitaminosis, and consequently originates a conditioned deficiency—that is, one in which the intake of vitamins proves insufficient because of some abnormal condition in the body.

Finally, in view of the ready precipitation of the A and B avitaminosis disease by pregnancy, or by an excess of carbohydrate in the diet, it is interesting to recall that the pituitary hypertrophies during pregnancy. Two of its hormones, pitocin and pitressin, contain sulphur in their molecule, and insulin is a rich sulphur-containing substance.

Disease Caused by Excess Cereal in the Diet

The Freetown Gaol is a relatively up-to-date building of concrete, with a population of between 200 and 250 African prisoners, and provided with a kitchen in which all the cooking is done by steam. The dietary of the prisoners is as follows, on alternate days.

First Day:

Morning.—Rice, 12 oz.; raw fish, 2 oz.; greens, 3 oz.; salt, $\frac{1}{4}$ oz.; palm oil, 1 oz.; beef or mutton, 1 oz., minced.

Evening.—Rice, 10 oz.; minced meat, 1 oz.; greens, 3 oz.; salt, $\frac{1}{4}$ oz.; palm oil, 1 oz.; pepper, $\frac{1}{20}$ oz.; kalandah, $\frac{1}{40}$ oz.; onions, $\frac{1}{4}$ oz.; limes.

Second Day:

Morning.—Foo-foo, 1 lb.; minced meat, greens, salt, palm oil, pepper, kalandah, and onions (weights as above).

Evening.—Rice, 10 oz.; two-thirds of a dried bonga; greens, salt, palm oil, pepper, onions, limes, kalandah (weights as above).

Cocoa, $\frac{1}{2}$ oz., sugar, $\frac{1}{2}$ oz., daily before morning work.
Fruit, twice a week.

A large number of prisoners on admission to the gaol show evidence of the epithelial and mucous membrane lesions of the A and B avitaminosis disease, and it has been observed that in most cases the prison diet effects a cure of these lesions, but not so rapidly as when vitamin therapy is instituted.

The prison bakery, which was established to supply outside Government institutions, is staffed by long-sentence men. These men, when drafted to the bakery, do not show any evidence of the disease, but after some time there they are noticed to develop the epithelial lesions; whereas men in all the other branches—namely, tailoring, sail-making, rice mill, stone sheds, etc.—as a rule remain free when once well. It is very significant that all the men in the bakery should show evidence of the disease, whereas it is hardly to be found among the rest of the gaol population. The only explanation of this fact is that the bakers are allowed $\frac{1}{2}$ lb. of bread a day—they certainly eat much more—in addition to their usual diet. It is presumed that this extra carbohydrate intake is sufficient to unbalance the diet and precipitate the disease.

For a period there were five bakers under observation; when it was decided to treat them they were left under the same dietetic conditions which, it is presumed, caused the disease to develop, and their condition was as follows:—

Patient	Tongue	Angles of mouth	Scrotum
No. 1..	Shiny	Slightly altered	Typical powdery condition
No. 2..	Shiny and tremulous	Altered	Well marked
No. 3..	Slightly shiny	Slightly altered	Typical powdery condition
No. 4..	Normal	Thick white fur	Typically altered where contact with penis
No. 5..	"	Slightly sore	Normal

The following shows the treatment given and results obtained:—

Patient	Treatment for 14 Days	Result
No. 1..	Radiostoleum injection 2 c.cm. daily	Improved
No. 2..	Marmite, $\frac{1}{2}$ oz. daily	Scrotum improved; tongue and mouth practically well
No. 3..	Radiostoleum injection 2 c.cm. daily	Scrotum well; tongue and mouth practically well
No. 4..	Marmite $\frac{1}{2}$ oz. daily	Scrotum improved; angles of mouth not much improved
No. 5..	Cod-liver oil daily	Not much improved

At the end of fourteen days they were all placed on $\frac{1}{2}$ oz. of marmite and 2 c.cm. of radiostoleum daily for a further six days, and at the end of the period they were all quite free from evidence of the disease. This observation shows that the condition can be precipitated by unbalancing the diet without the addition of a prussic-acid-containing substance, can be improved by increasing either the vitamin A or vitamin B intake, and be more readily cured by the administration of both vitamins together.

Asulphurosis

I. Sabry (1931), in a paper "On the Chemical Nature of the ' Pellagra Toxin ' and the Discovery of the Thiosulphate Treatment of Pellagra," reported his discovery that sodium thiosulphate would cure cases of human pellagra, which he considered to be due to the affinity of the drug for a toxic substance which was the cause of the disease.

In a recent paper on the aetiology of pellagra and allied nutritional diseases, A. Clark (1935) states that prussic-acid-containing foods, such as cassava, maize, sugar cane, millet, guinea corn, peas, and beans, are a common factor present in the diet of all patients suffering from these diseases. He adds that prussic acid combines with sulphur to form thiocyanic acid; the urine and saliva of pellagrins contain a greater amount of thiocyanate than that of non-pellagrins. He has shown experimentally that fatty degeneration of the liver in rats is a constant sequel to the administration of prussic acid or nitriles in sublethal quantities, pointing out that fatty degeneration has been a common finding in the pellagra-like diseases. He postulates

that pellagra and its allied diseases are due to slow prussic acid poisoning, and asks "Is sulphur the P. P. factor?"

Hawk and Bergeim (1931) state that potassium thiocyanate is generally present in the saliva to the extent of several milligrams per cubic centimetre. It has been claimed that this substance is present in greatest amount in the saliva of habitual smokers. The significance of thiocyanate in the saliva is not known; it probably comes from the ingested cyanides present in certain fruits and in tobacco smoke, and from the breaking down of protein material. When 100 grams of tobacco as cigarettes is burned it yields 0.08 gram of hydrocyanic acid (Martindale and Westcott, 1932).

Failure of vision is only an occasional result of the excessive consumption of tobacco, a failure less likely to occur, or more readily cured, if smoking is only indulged in on a full stomach (G. A. Berry, 1893). This is an important observation when considering Clark's theory of slow prussic acid poisoning in the pellagra-like diseases, for it strengthens the supposition that there is a fault in the organism rather than a fault in the ingested material. This supposition is further strengthened by the knowledge that recovery may take place without any change of habit with respect to smoking.

Hawk and Bergeim (1931) remark that the metabolism of sulphur in the body is primarily the metabolism of cystine. The daily sulphur requirement of the body is probably in the neighbourhood of one gram, and is ordinarily supplied when the protein requirement is safeguarded. The sulphur content of foods may be considered as approximately 1 per cent. of the total protein content. It becomes apparent, then, that the diet should contain 100 grams—that is, 3½ oz.—of protein daily in order to satisfy the sulphur requirements of the body; this amount should contain some of the good-class proteins. Generally speaking, the diets in Sierra Leone do not come up to this standard, and are consequently deficient in sulphur.

Randoin and Fabre (1931) have shown that a diet deficient in the vitamin B complex fed to rats caused a fall of the thiol-derivative (sulfhydryl) content of muscle and liver and a rise of these substances in blood. The interpretation of this experiment suggests that either sulphur is mobilized from muscle and liver in the absence of vitamin B or that the organism is unable to metabolize sulphur properly in the absence of vitamin B.

It was decided to use sulphur as a therapeutic agent in the treatment of the A and B avitaminosis disease in Sierra Leone. Contramine (diethyl-ammonium-diethyl-dithiocarbamate) was chosen as a suitable organic sulphur compound. The usefulness of sulphur in the form of contramine by injection being proved, it was decided to use ichthyol, which has a high sulphur content, in further experiments, all of which are detailed below. This drug was only used orally, although it can be given parenterally.

Case 1.—A policeman was admitted to hospital on February 25th, 1936, suffering from avitaminosis—evidenced by a glazed tongue, altered angles of the mouth, and an eczematous, dry, irritable scrotum. He was given full diet and a daily injection of 0.125 gram contramine for four consecutive days; by March 2nd, within a week, the epithelial lesions were cured. This case is cited because it was the first one treated with sulphur, but the result is not conclusive, because there were no dietary restrictions.

Case 2.—A destitute man, an old case of avitaminosis, who had been treated and cured some five years previously with a liberal diet, radiostoleum, and marmite, was admitted to hospital on March 9th, 1936. His tongue was completely glazed; there was some conjunctivitis, and the lower lids of both eyes and the inner and outer canthi were altered. The scrotum was dry, with the rugae completely absent, and appearing as though the skin would easily break. The under surface of the penis was also involved.

He was placed on a strict diet of bread, rice, arrowroot, and beef-tea, daily. No milk or butter was allowed throughout the treatment, and no bathing or local treatment was permitted. He was given daily, on March 9th, 10th, and 11th, injections of contramine 0.125 gram, and on March 12th and 13th an injection of 0.25 gram contramine, making a total of 0.875 gram of the drug. No further treatment was given. There was steady improvement until March 13th, but by March 16th it was apparent that the healing process was stationary; the scrotum had healed completely in the upper two-thirds of its surface, but the lower third remained unhealed in the form of a cap. On this day, March 16th, the patient was given half an ounce of cod-liver oil, with the addition of 10 minims of radiostoleum, and half an ounce of marmite daily; in three days all the lesions were healed.

Case 3.—A seaman was admitted to hospital on April 8th, 1936, suffering from avitaminosis, evidenced by a completely glazed tongue, sore angles of the mouth, the scrotum in a typical eczematous condition and the skin of the lower abdomen, portions of the neck, and back very dry and corrugated; he also had defective vision. He gave a history of having proceeded to sea on March 1st, 1936; during the latter part of the month he felt some vague rheumatic pains, after which the condition just described slowly developed. He was at sea thirty-eight days, and fed on rice, biscuits, and soup. He came straight to hospital from the ship.

He was given a strict diet of arrowroot, bread, and beef-tea; no bathing and no local treatment were allowed during the period of observation. Treatment was started on the day of admission, with ichthyol, 30 grains, in peppermint water, morning and night. The tongue, angles of the mouth, and the scrotum were completely healed, and the vision was normal by April 16th—that is, in eight days.

The following series of cases were observed at the Free-town Gaol:

Case 4.—A male adult was admitted to prison on March 2nd, 1936. In this patient the epithelial lesions were well marked, his tongue was completely glazed, and the angles of the mouth were crusted, sodden, and white; the outer canthi of eyes showed the typical alterations. The whole of the scrotum was in a dry, furfuraceous condition. He was placed in the prison hospital on the same day, and was given a diet composed of the following items: bread, 12 oz.; sugar, 2 oz.; arrowroot, 1½ oz.; sago, 2 oz.; and beef soup, 10 oz. No bathing and no local treatment were permitted. On March 2nd, he was given an injection of contramine 0.125 gram, and his condition gradually improved up to the 4th. By March 5th, the same treatment having been continued daily, the epithelial lesions were markedly improved. On March 6th no treatment was given, but the patient continued to improve. On March 7th no treatment was given, but improvement continued. On the next day the scrotum became normal; the tongue had lost its polish, and the angles of the mouth and the canthi were healed.

Case 5.—A man admitted to prison on January 30th, 1936, was found to be suffering from very marked epithelial lesions, for which he was given vitamin treatment up to February 29th, when he was completely cured. On April 7th he reported with a recurrence of the condition, the scrotum, mouth, and tongue lesions being present. He continued as an out-patient in the same conditions under which he had relapsed, but was given 40 grains of ichthyol twice a day. Steady improvement took place, so that by April 16th the scrotum was quite cured, and the mouth and tongue were almost well. On April 20th there was no trace of the disease.

Case 6.—A man entered prison on March 24th, 1936, with marked epithelial lesions of the disease. He was admitted the same day to the prison hospital, and placed on the same diet as Case 4. The patient was treated with daily injections of 0.125 gram of contramine for four doses. The first injection was given on the 24th, and afterwards the result was as follows:

March 26th. Marked improvement in the scrotum; the mouth and tongue only slightly improved.

March 27th. The scrotum almost completely cured; the mouth and tongue still the same.

March 28th. The scrotum normal; the mouth and tongue definitely improved.

Case 7.—A man was admitted to prison on March 4th, 1936; he was a very marked case of epithelial lesions, the tongue being glazed, the angles of the mouth sore, the scrotum and under surface of the penis involved, and the eyelids affected. He gave a history of three months' duration. He was admitted to the prison hospital on the same day, and placed on the same diet as Case 4. No bathing or local treatment was allowed. The sequels were:

March 4th. Injection with 0.125 gram of contramine was repeated daily for four doses, so that by

March 7th there was considerable improvement. On

March 8th the condition was further improved.

March 10th. The fifth injection of 0.125 gram of contramine was given.

March 11th. The sixth injection of 0.125 gram of contramine followed and there was steady improvement.

March 13th. He was cured.

Case 8.—A man, admitted to prison on April 8th, 1936, was found to be suffering from marked avitaminosis affecting the tongue, angles of the mouth, and the scrotum. He was admitted to the prison hospital on the same day, and was placed on the same diet as Case 4. No bathing or local treatment was allowed.

April 8th. Dose of 40 grains of ichthyol given.

April 9th. Dose repeated.

April 10th. Dose repeated. The scrotum was now nearly well, but there was not much improvement in the tongue and mouth.

April 11th. Ichthyol to the amount of 80 grains in divided doses was given. The scrotum was nearly well; not much improvement was seen in the tongue and mouth.

April 12th. Ichthyol, 80 grains, was given in divided doses; the scrotum was nearly well and there was slight improvement in the tongue and mouth.

April 13th. Dose of 40 grains of ichthyol given. The scrotum was healed, and there was slight improvement in the tongue and mouth. The patient was discharged from gaol.

Case 9.—A man was received at prison on September 17th, 1935, in ill-health with bronchitis, urethritis, and chronic ulcer of leg, all of which were treated and cured. He developed avitaminosis on April 11th; scrotum, oral, and tongue lesions were present. The scrotum had lost all its rugae and was "weeping" and painful so as to hinder walking. He continued as an out-patient on the same diet and under the same conditions which caused the relapse, but was placed on ichthyol (40 grains in peppermint water twice daily), starting treatment on April 11th.

April 13th. Slight improvement was noticed in the scrotum; the mouth and tongue were unchanged.

April 16th. The scrotum was still improving, and the mouth and tongue were greatly improved.

April 18th. The scrotum was better, and the mouth and tongue were almost well.

April 20th. Ichthyol in 40-grain doses given thrice daily.

April 22nd. The scrotum, mouth, and tongue were healed.

Case 10.—A man admitted to prison on May 4th, 1936, was found to be suffering from the epithelial lesions of avitaminosis. The tongue was partly glazed; the angles of the mouth were in the typical condition; and the scrotum showed a well-marked eczematous condition extending on to the under surface and dorsum of the penis near the glans. The genital condition showed slight weeping. The patient was admitted to the prison hospital on May 4th, a photograph was taken of the condition to illustrate the case before treatment, and he was then placed on the restricted diet recorded in Case 4. No bathing and local applications were allowed, and the only treatment was as follows:

May 4th. Injection with 0.125 gram of contramine intramuscularly.

May 5th. Injection of 0.25 gram of contramine. Slight improvement was noted.

May 6th. Injection of 0.25 gram of contramine. The improvement continued.

May 7th. Injection of 0.125 gram of contramine. There was considerable improvement in the scrotum and penis; the mouth and tongue were still improving.

May 8th. Injection of 0.125 gram of contramine. The scrotum and penis were almost well; the tongue was considerably improved; and the mouth was gradually improving.

May 9th. A photograph was taken to show the result of this treatment.

This observation only lasted five days on account of the author's departure from the prison department. The patient was kept on the same regime and no further treatment given until the third photo was taken on May 12th, but, nevertheless, the improvement was sufficiently striking to be seen in the illustrations. The dorsum of the penis was the site of scabies, and has not healed as has the scrotum.

The response of some of these cases to sulphur therapy gives an indication of its possible mode of action.

Case 2 was a destitute and relapsed case of A and B avitaminosis disease, placed on a very poor diet. Nevertheless, it responded to sulphur treatment in the form of contramine parenterally, but the cure was not completed until cod-liver oil and marmite were added to the diet. The inference to be drawn here is that a body deficiency of sulphur rendered these vitamins present in the body impotent. The administration of sulphur enabled the body to benefit from the presence of these vitamins until available stores were all used up, when their administration became necessary to complete the cure.

Case 3 demonstrates the development of the A and B avitaminosis disease without one of the prussic-acid-containing foods being present in the diet. Particularly interesting is the cure of his defective vision with ichthyol whilst on a poor diet.

Case 5 shows the cure with sulphur of a relapsed case, while continuing on the diet and under the same conditions in which the relapse occurred.

Case 8 showed only slight improvement in the tongue and mouth, although the scrotum healed, but it should be noted that this patient was only under observation for five days. The general impression gained whilst observing these cases was that the scrotum yielded to treatment first.

It might be suggested that sulphur is a well-recognized therapeutic agent in the treatment of many skin diseases. In fact, Landor and Pallister (1935) state: "Professor Rosedale has kindly permitted us to say that in a recent experiment on the feeding of rats on vitamin B₁ deficient diets he found a mangy condition of the fur develop which, however, could be cured by the local application of eight parts rape oil with one part of black sulphur." It remains to be explained how sulphur causes the regeneration of the denuded surface epithelium of the tongue and the restoration of visual acuity. It is also very significant that a rich supply of end-bulbs is found in the synovial membranes lining joints, in the intestinal mucosa, and in the sheaths of nerve trunks. In the A and B avitaminosis disease vague joint pains are frequently felt, epigastric discomfort is a constant symptom, and neuritis is a feature of its late or nervous stage.

Conclusions

- i. Vitamins A and B are interdependent for their efficient functioning.
- ii. An excess of a cereal, not containing a cyanogen group, added to a balanced diet can precipitate the A and B avitaminosis disease.
- iii. Vitamins A and B can remain inactive in the organism if its sulphur content falls below a certain level.
- iv. Great benefit to the patients and economy in treatment results from judicious sulphur therapy.

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HODGKIN'S DISEASE AND DEEP X-RAY THERAPY

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The total number of cases under review is 201. These have been treated between the years 1923 and 1934. The great majority of the patients are hospital cases who from the precarious nature of their occupation and living are not infrequently lost sight of and cannot be traced. These cases are simply shown as alive up to the time when last seen, so any comparative statistics given are the minimum, and with fuller knowledge would naturally be higher. My grateful thanks are extended to the members of the staff and others for the great help given in treating and following the cases.

Analysis of Cases

The disease attacks approximately two males to one female. The primary symptoms where known are as follows:

	Cases		Cases
Right cervical	43	Jaundice	1
Left cervical	38	Facial paralysis	1
Right axilla	8	Tonsil	2
Left axilla	2	Herpes	1
Right inguinal	5	Sciatica	2
Left inguinal	4	Purpura	1
Abdominal	7	Appendicitis	1
Pyrexia	6		

Various structures of the body were definitely affected as follows at some time or other in the course of the disease:

	Cases		Cases
Liver	11	Sternum and sterno-clavicular	5
Spleen	49	Spine	12
Breast	10	Hip	2
Mediastinum and lungs	76	Humerus	1

The spleen where affected is usually just palpable. The breast shows a diffuse infiltration and may be twice the

size of the other. In one case there was ulceration. In the mediastinal cases eight were massive, filling the chest cavity. Twenty-three only showed enlarged hilum glands. In the spinal cases two distinct conditions are present: one a definitely encapsulated tumour in the spinal cord itself, the other a subacute destructive osteitis of the vertebrae themselves. The latter is usually accompanied by severe pain.

The cervical, axillary, and inguinal glands are the ones most affected; of the others, one or both parotids, the occipital, submental, or epitrochlear are occasionally enlarged, and in one case the popliteal.

Clinical Features

Asthenia is the prominent symptom in most cases. It is associated with an anaemic appearance out of all proportion to the blood picture. Typical blood reports are as follows:

Case	Haemoglobin	Red Blood Cells	Leucocytes	Polymorpho-nuclears	Lymphocytes	Eosinophils
	per cent.					per cent.
1	67	4,300,000	8,600	—	—	2.0
2	90	4,000,000	11,200	69	22	2.0
3	77	4,600,000	13,000	76	18	1.5
4	63	4,000,000	16,000	86	10	2.5
5	81	4,500,000	13,000	72	14	2.0
6	80	4,000,000	8,000	62	35	2.0

Atypical blood reports:

7	77	4,600,000	15,000	40	16	39.0
8	90	4,200,000	6,500	—	—	3.5
9	68	—	8,500	—	—	5.0
10	62	3,900,000	38,000	70	12	11.0
11	80	4,600,000	8,000	61	25	6.5
12	45	3,200,000	12,200	38	22	35.0

In the typical case we have a marked drop in the haemoglobin, otherwise a more or less normal blood picture except that there is usually a mild leucocytosis. In certain cases—especially the abdominal, where the iliac and pelvic glands are affected—we may get a marked eosinophilia, as illustrated, and in doubtful cases this may be of diagnostic importance.

Pyrexia is at times the outstanding feature of the case and may persist even when all discoverable glands have disappeared under treatment. It will have been noticed under primary symptoms that the right and left cervical glands are not only by far the most frequent but that they are practically equally affected. The proportion of mediastinal involvement is, however, altogether different; twice as many cases are affected when the right is the primary side than when the left comes first. If any glands are found present, with full treatment and disappearance the temperature may rapidly subside to normal. In two cases the discovery of glands in the upper abdomen explained the cause of the persistent pyrexia. In one case the spleen appeared to be the sole cause.

Abdominal glandular enlargements may be primary or secondary. If primary and the iliac glands are affected oedema of one or both legs may be the first symptom, if the aortic glands, acute obstruction of the bowels may be the first sign. In one case this was found and relieved at operation, in the other it was suspected as a late symptom and was relieved by irradiation. In one case