denied until 1871, when C. E. Brown-Séquard, on experimental grounds, argued that lesions of the pons caused haemorrhages, and injuries of the medulla oblongata oedema of the bases of the lungs as a result of impulses transmitted through branches of the sympathetic leaving the cord in the upper dorsal region. Rose Bradford and Dean (1889, 1894) found that in the dog vasomotor nerve fibres derived from the upper dorsal nerve supply the pulmonary blood vessels, though the pulmonary vasomotor mechanism is poorly developed as compared with that regulating the systemic arteries. They also concluded that the pulmonary circulation is comparatively independent of the systemic, and that alterations in the blood pressure of the latter must be so considerable as to interfere with the action of the cardiac valves and produce regurgitation before affecting the pulmonary blood pressure. On the other hand, Brodie and Dixon, in 1904, denied the vasomotor control of the pulmonary circulation, and in 1928 Dixon and Hoyle confirmed this. In the meanwhile Führer and Starling, using the heart-lung preparation, found a considerable degree of pulmonary vaso-constriction and a rise of pulmonary arterial pressure with adrenaline, and in 1905 François-Franck came to a similar decision. In a critical review of the extensive work on the subject Wiggers, in 1921, concluded that reflex vasomotor effects on the pulmonary circulation must be regarded as probable rather than proved.

The *intracranial circulation* is remarkable for the rigid cranial cavity and the water-bed of the cerebro-spinal fluid. Whether or not the nerves accompanying the cerebral vessels exert a vasomotor function has been repeatedly investigated, but with discordant results; Roy and Sherrington (1890), L. Hill (1896), and more recently Florey (1925) who found that the cerebral arteries and the cerebral ends of the capillaries react to mechanical, thermal, electrical, and chemical stimuli by contraction and dilatation, agree that there is not any evidence of nervous control over the cerebral vessels. On the other hand, the existence of active functional control of the cerebral vessels by vasomotor nerves has been supported by Claude Bernard (1858), Nothnagel (1867), Wiggers (1915), Forbes and Wolff (1928), and others. The experimental observations are of much interest in connexion with the belief held by many clinicians that transient paralyses, such as occur without evidence of a gross lesion, may be due to spasm of the cerebral arteries analogous to that in Raynaud's disease. Osler (1911), in describing transient attacks of aphasia and paralysis in states of high blood pressure and arterio-sclerosis, accepted the view put forward by Peabody (1891), W. Russell (1909), and others that they were due to transient spasm. Florey has thrown out the suggestion that possibly in pathological conditions, such as arterio-sclerosis, an abnormal metabolic product which has not any effect on normal blood vessels may produce spasm of damaged arteries.

The influence of the conditions of the cerebral circulation on the general blood pressure has been much discussed. Starling and Anrep (1925) showed that when imperfectly supplied with blood the vasomotor centre brings about a compensatory rise of blood pressure, thus confirming Cushing's earlier demonstration in 1901 that the vasomotor centre exerts a regulating influence whereby anaemia of the medulla oblongata is prevented when the intracranial pressure is increased above that in the cerebral vessels. This was supported by Bordley and Baker's (1926) observation that in arterio-sclerosis a high blood pressure was definitely associated with sclerosis of the arterioles of the medulla; this, however, was contested by Keith, Wagener, and Kernohan, and Cutler's observations showed that gross vascular changes in the blood supply to the medulla were not responsible for blood pressure changes. Experimentally Florey, Marvin, and Drury (1928) found that lowering the blood pressure in the circle of Willis has not any influence upon the general blood pressure.

ON RECOVERY FROM SYMPTOMS OF INTRACRANIAL TUMOUR.

BY

C. O. HAWTHORNE, M.D.GLASG., F.R.C.P., F.R.F.P. AND S.,

CONSULTING PHYSICIAN, HAMPSTEAD AND NORTH-WEST LONDON GENERAL HOSPITAL AND CENTRAL LONDON OPHTHALMIC HOSPITAL.

THAT an intracranial tumour can exist without distinctive symptoms, and even without suggestive symptoms, is a proposition that has for its warrant the sure teaching of experience. Again, it is well recognized that even when symptoms of tumour are present there is often, in the course of one and the same case, a wide variation in the degree of their severity, and, indeed, a period of quiescence may be so prolonged and so pronounced as to cast suspicion on the accuracy of the diagnosis. The explanation of such experiences is that for the most part the symptoms associated with intracranial tumour are due less to the mass of the tumour than to circulatory disturbances (congestions, anaemias, oedemas, haemorrhages, softenings) liable to occur in its neighbourhood, and to interferences which the tumour may exercise on the circulation of the cerebro-spinal fluid. Grant the absence of these accidents, and cerebral events and symptoms, in spite of the presence of a tumour, may be slight, non-suggestive, and even non-existent.* With these positions admitted, may it not be possible that symptoms, and even pronounced symptoms, of intracranial tumour may disappear, not merely for a more or less brief period, but completely and permanently? For if in an individual case the intracranial accidents or complications, and the symptoms which result from these, may after a period of activity subside, the possibility that such quiescence may be permanent can at least be contemplated. Assume that the tumour ceases to grow or perhaps shrinks in size, and that in this or in some other fashion it no longer causes the intracranial disturbances on which the clinical evidences of tumour mainly depend, and it is no violent proposal to suggest the possibility of a clinical record in which the symptoms of intracranial tumour disappear completely and the patient regains a level of good health. The clinical history, unfortunately, marches usually in the opposite direction, but there is nothing in the nature of things to render exceptions to this rule impossible, and the principal object of this communication is to suggest that such exceptions do actually occur. This suggestion has for its support case records (admittedly exceptional) marked in the earlier stage by symptoms regarded as conclusive of intracranial tumour, while later these symptoms disappear and the patient succeeds to good health. Such experiences, of course, call for an explanation, and the explanation here proposed is cessation of intracranial disturbances consequent on quiescence or shrinking of the tumour growth.

That recovery from symptoms of intracranial tumour, except for blindness due to optic atrophy, actually occurs there can be no doubt. Records of patients who in earlier years have suffered a severe illness characterized by headache, vomiting, and optic neuritis, and who, but for loss of sight, have later made a good recovery, are well established. It may be suggested that these cases are not cases of tumour, and it must be admitted that in exceptional instances the symptoms just quoted have existed and yet no tumour has been found on *post-mortem* examination;[1] such conditions as hydrocephalus,[2] serous meningitis,[3] or sinus thombosis[4] may perhaps be advanced as alternatives to tumour. On the other hand, in many patients who are blind from optic atrophy after an illness distinguished by cerebral symptoms, competent clinical observers present at the time of the original illness have felt no doubt that the symptoms meant intracranial tumour; and now and again in the brain of a patient included in this group, and dying years after the primary illness, a tumour has been present to *post-mortem* demonstration. Thus it is certain that within the natural history of intracranial tumours room must be found for cases in which all active evidences of the presence of a tumour disappear, the former cerebral disturbances being

* A recent example is reported by Professor Sydney Smith, *British Medical Journal*, January 22nd, 1927.

indicated only by blindness due to optic atrophy consequent on the earlier double optic neuritis. Clinical records of this order can be found in the writings of Jonathan Hutchinson, Hughlings Jackson, and others, and some years ago I published a detailed study of a number of such cases.[5]

The usual story is of a severe and more or less prolonged illness which occurred in early life and was followed by recovery qualified by blindness; and examination shows atrophic optic discs. In some instances this is all, while in others there are, in addition to the blindness, such other evidences of cerebral disturbance as ocular or facial palsies, unilateral motor weakness, abnormalities of the tendon jerks or of the superficial reflexes. Again, some of these patients are liable to quasi-epileptic seizures or to mental instability; and individual instances have been noted in which, after a more or less prolonged period of good health, active and alarming symptoms of cerebral disturbance have recurred, followed by death or occasionally by a second recovery. The immediate point relative to the present argument is that after an illness having symptoms which suggested or even compelled the diagnosis of intracranial tumour, the patient, but for blindness the result of consecutive optic atrophy, may apparently get quite well and may remain well for years. Every now and again such an experience is described in the medical journals, and more or less numerous examples have been collected by the authorities already quoted. Two recent cases may be summarized as illustrations.

CASE 1.

Thos. W., aged 65, admitted to hospital with left-sided pleurisy. He is blind and the optic discs are conspicuously atrophic. His loss of sight is attributed to a serious illness which lasted for two years when he was 8 to 10 years of age; with this exception he has had good health.

CASE 2.

Ellen C., aged 45. When 18 she had "a heavy illness" of some twelve months' duration and characterized by headache, vomiting, and double vision. Since this she has been blind, but has had fair general health interrupted occasionally by headache. Examination shows consecutive optic atrophy and paralysis of the left external rectus, but no other evidence of disease.

In Case 1 recovery is complete but for optic atrophy; in Case 2 there is, in addition to the optic atrophy, an ocular paralysis and some recurrence of headache. A *post-mortem* demonstration that cases such as these are really cases of intracranial tumour cannot often be obtained. Yet even this degree of evidence is not altogether wanting, and records of a few such cases have been completed by the discovery of a tumour at the *post-mortem* examination. A very impressive experience of this order is described by J. R. Lunn[6]—namely:

CASE 3.

A man, aged 27, was admitted to Marylebone Infirmary in October, 1887, with a story of failing eyesight and severe headaches since Christmas, 1886. The left eye was quite blind and the disc pale; the right eye was nearly blind and receding optic neuritis was present. He lived for seventeen years in the infirmary without symptoms of active disease, except on two occasions a "fit" attended by unconsciousness; he died after a similar seizure in 1904. *Post-mortem* examination disclosed a fibrocystic tumour the size of a pigeon's egg in the interpeduncular space and involving the optic chiasma.

A parallel case is recorded by Professor T. K. Monro.[7] The patient was blind for thirty-seven years after the original illness; a myxomatous tumour was found in the cerebellum. In another instance, described by Dr. Lloyd Roberts,[8] there was, eight months after recovery from the original illness, a recurrence of the cerebral symptoms, followed by death; but in the interval the patient, though blind, had been "perfectly well." *Post-mortem* examination discovered a glioma of the cerebellum.

From such experiences it is manifest that an illness accompanied by severe cerebral symptoms, including bilateral optic neuritis, and followed by disappearance of all the symptoms except blindness due to optic atrophy, may have as its explanation the existence of an intracranial tumour. Presumably the tumour shrinks or ceases to grow and so no longer causes the circulatory and allied disturbances which are the immediate causes of the clinical symptoms associated with intracranial tumours. The proposal now made is that in rare instances this cessation of tumour activity may be accompanied, not only by cessation of headache, vomiting, and the rest, but also by subsidence of the optic neuritis without damage to the optic nerve fibres, and consequently without prejudice to vision. In support of this proposition there are here submitted six case summaries—namely, one in which optic neuritis disappeared for some three years and then recurred, and the *post-mortem* examination revealed an intracranial tumour; one where the optic neuritis and other symptoms disappeared under antisyphilitic treatment; and four examples of complete recovery from symptoms (including bilateral optic neuritis) regarded by experienced observers as indicative of intracranial tumour.

CASE 4.

A man (F. W.), aged 62, when first seen in 1916 had suffered for four years from occasional "giddy attacks," and in some of these had fallen to the ground, but had never lost consciousness; there were no objective signs of disease and no optic neuritis, and an aural surgeon reported nothing beyond "slight dry catarrh in middle ear." At the end of 1917 "attacks" had continued, and there was definite exudation at the right optic disc and some blurring of the edge of the left disc; the Wassermann test of blood and cerebro-spinal fluid was negative. In March, 1919, he reported himself as much better; general examination was quite negative, and the optic discs were regarded as normal. Early in 1920 he had a severe "attack" of giddiness with apparent unconsciousness (no convulsions) lasting some fifteen minutes; there was extreme optic neuritis in the right eye, less in the left. The skull was trephined, but the patient died a few days after the operation; a firm fibrous tumour the size of a large cherry was adherent to the right petrous bone.

The feature of the case particularly relevant to the present communication is the disappearance, for a time at least, of the optic neuritis without damage to vision, though, as shown by the subsequent facts, the neuritis was undoubtedly caused by an intracranial tumour.

CASE 5.

A woman (A. H.), aged 27, was admitted to hospital with a history (three months) of severe headache, vomiting, and, recently, of double vision. Vision was 6/12 in each eye; there was extreme swelling of each optic disc, and paresis of the external rectus of the left eyeball; the Wassermann test was positive; examination showed nothing abnormal in other respects. There was prompt improvement under treatment. Seen two years later she was in good health; the optic discs were whitish, with traces of former exudation; vision (each eye) 6/6.

The disappearance under appropriate treatment of clinical signs of intracranial specific disease is, of course, a familiar experience. But in the present series Case 5 takes its place as a proof that optic neuritis due to an "adventitious product" within the skull may disappear when the activity of the intracranial cause is reduced; and also, that optic neuritis so removed may leave vision intact. If this is true when the "adventitious product" is a specific mass, may it not be true also of other pathological masses—for example, tuberculoma? The three records quoted under "Case 3" would seem to give an affirmative answer.

CASE 6.

A woman (Mrs. T.), aged 46, seen with Dr. Gavin Barbour in October, 1920. She had complained for six months or so of severe headache which often prevented sleep, and recently of dimness of vision; no vomiting. There was extreme exudation at each optic disc; no other objective sign of nervous disease was present, and the blood serum and cerebro-spinal fluid gave a negative Wassermann reaction. In 1922 the patient reported herself well; the optic discs were white, but there was no swelling. Vision: right eye 6/6, left 6/18 (extreme myopic astigmatism), 1928: well, and active social worker.

Whether this is or is not a case of tumour, the record certainly shows that a severe degree of exudation at the optic disc (regarded as due to tumour) may be absorbed and vision be left unimpaired.

CASE 7.

A woman (E. C.), now (1928) aged 35, was from May to August, 1908, an in-patient in the National Hospital, Queen Square, with a history of attacks of pain in the head, giddiness, and vomiting extending over two years; there was considerable exudation at each optic disc. Vision, each eye (with myopic correction), 6/9. The case was indexed as "intracranial tumour, infratentorial, (?) left cerebellar."* The symptoms ceased (except for one attack) during residence, and the patient was instructed to return should there be any further attacks.

March 1st, 1921. Seen with Dr. R. D. Bell of Luton. The patient had worked as a milliner since leaving the hospital; she had occasional headaches, and in 1915 was ill for six months with attacks of pain in the head, giddiness, and vomiting; she recovered, and was at work again until two months ago, when headache and giddiness were again troublesome; the optic discs

*I am indebted to the courtesy of Dr. Macdonald Critchley, the medical registrar, for the opportunity of seeing the original notes.

looked suspicious, but were not swollen; no suggestion of atrophy. Vision (with glasses) 6/9 each eye; no contraction of visual fields. In other respects there were no signs of organic disease.

August 31st, 1928. Patient attended for examination by request. She was able to continue to work, and examination showed her general condition and the ophthalmoscopic facts to be the same as in 1921.

In a word, a patient regarded in 1908, and by an experienced physician, as undoubtedly the subject of an intracranial tumour, is in 1928 in fair general health, and the former optic neuritis has disappeared without leaving optic atrophy as its sequel.

CASE 8.

A boy (J. L.), aged 9 years, seen with Dr. Meikle in February, 1924, gave a history of attacks of severe headache, sometimes attended with vomiting, extending over three months; recently diplopia and dimness of vision and "weakness" of the left upper limb. Examination showed much exudation at each optic disc; vision (each eye) 6/9 part; paresis of the right external rectus and of the left lower face. He was admitted to hospital with a view to operation, but gradually the headache and vomiting ceased, double vision disappeared, and there was obvious recession of the swelling of the optic discs. In the end, the boy left the hospital apparently quite well. Seen in November, 1925, his weight had increased from 5 st. 1 lb. to 7 st. 7 lb.; his mother described him as "in perfect health." Examination was negative except that the optic discs were unduly white; vision (each eye) 6/6. In August, 1928, Dr. Meikle reports him to be "perfectly well."

In the early stage of this case there seemed no possible escape from a diagnosis of intracranial tumour. Does the completeness of the recovery and the persistence of good health qualify this conclusion? If not, then the case illustrates the proposition advanced in this communication—namely, that recovery from symptoms of intracranial tumour, when it occurs, may proceed to such a level as to include resolution of an optic neuritis and retention of a full standard of vision.

CASE 9.

A boy, aged 6, was seen in May, 1894, by Mr. Charles Higgens[9] on account of failure of sight; vision was found to be much depreciated; there was exudation at each optic disc. He was later seen by Dr. (afterwards Sir David) Ferrier, who recognized double optic neuritis and symptoms of cerebellar disease, and regarded the case as one of tumour. After this the boy was reported to have "gone blind," but when re-examined in 1907 by Mr. Higgens the visual acuity in each eye was 6/6 and the optic discs, though pale, were otherwise normal.

When these case records are subject to examination as a whole it would appear that in Cases 1, 2, and 3 symptoms of intracranial tumour disappear except for blindness due to optic nerve atrophy, while in Cases 6, 7, 8, and 9 similar symptoms are followed by complete recovery, and the reliability of the recovery is certified by freedom from symptoms for a term of years. Except in the degree of recovery attained, there does not appear to be any reason to draw a distinction between the two groups, and Cases 4 and 5 may be quoted as emphasizing the identity of the pathological basis on which the several cases rest. Hence it would appear that the facts as here collected and quoted justify the following conclusions:

1. That headache, vomiting, and allied symptoms indicative of intracranial tumour may cease, the patient, however, remaining blind from optic nerve atrophy (Cases 1 and 2).

2. That in some of these cases *post-mortem* examination years after the original illness has shown the presence of intracranial tumour (Case 3, References 7 and 8).

3. That in cerebral syphilis (presumably gumma) all the symptoms, including optic neuritis, may disappear, leaving the patient with normal vision (Case 5).

4. That, similarly, in occasional cases—non-syphilitic—symptoms of intracranial tumour, including optic neuritis, may disappear, leaving the patient with normal vision (Cases 6, 7, 8, and 9).

5. That whilst it is no doubt generally true that success in operations for intracranial tumour would be promoted by earlier diagnosis, the possibility of the natural subsidence of even pronounced cerebral symptoms ought not to be forgotten.

REFERENCES.

1 Tooth, Howard H.: *Brain*, 1912-13, vol. 35.
2 Purves-Stewart, Sir James: *Intracranial Tumours*, p. 184.
3 Idem, ibid., p. 187.
4 Hawthorne, C. O.: *Studies in Clinical Medicine*, pp. 115, 139. Garrod, Batten, and Thursfield: *Diseases of Children*, p. 804.
5 Hawthorne, C. O.: *Studies in Clinical Medicine*, p. 71.
6 Lunn, J. R.: *British Medical Journal*, June 16th, 1906.
7 Monro, T. K.: *Glasgow Medical Journal*, 1896, vol. ii.
8 Roberts, Lloyd: *Lancet*, November 15th, 1902.
9 Higgens, Charles: Ibid., September 21st, 1907.

VITAMIN A AS AN ANTI-INFECTIVE AGENT.

BY

H. N. GREEN, M.D., CH.B., M.Sc.,

AND

E. MELLANBY, M.D., F.R.C.P., F.R.S.

(From the Pharmacology Department, University of Sheffield.)

THE assigning of names descriptive of some particular function to distinctive vitamins has been a useful, although probably only temporary, step in the development of knowledge of these elusive entities, because their identification has so often depended upon the appearance of definite syndromes in animals whose diets have been deficient in certain respects. The use of the words "antiscorbutic," "antineuritic," and "antirachitic" in describing specific vitamins is an example of this, and from a clinical standpoint the nomenclature has been of great value. Vitamin A has always presented special difficulties to a clinically descriptive term because it has depended to such a large extent on a purely physiological criterion—namely, growth in young animals—for its detection. It is in consequence often referred to as the "growth-promoting" vitamin. Since the recognition of vitamin D (the antirachitic vitamin) as an entity distinct from vitamin A, those with experience of nutritional work have felt that to call vitamin A the "growth-promoting" vitamin is a misnomer, for good growth often takes place in its absence if the diet is otherwise complete. In fact, when growth ceases owing to the single absence of vitamin A from the diet, it often means that the animal is definitely ill—in the sense, as will be seen below, of its having developed some, and often a widespread, infective condition. Indeed, the present paper supplies evidence in favour of the term "anti-infective" being applied to vitamin A.

From the early days of its recognition it has been thought that vitamin A was concerned with resistance to infection, at least of a specific type. This is seen in its description as the "anti-xerophthalmic" vitamin, but this appellation has never become widely adopted, partly because xerophthalmia in human beings, although related to vitamin A intake as suggested by the observations of Mori[1] and shown by Bloch,[2] is of very rare occurrence, and partly because McCollum, Simmonds, and Becker[3] have shown that this eye condition results from dietetic abnormalities other than vitamin A deficiency.

Several workers, including Drummond,[4] Cramer and Kingsbury,[5] and Steenbock,[6] have commented on the susceptibility to lung infections of animals on vitamin A deficient diets. In the case of dogs E. Mellanby[7] drew attention to the development of broncho-pneumonia in animals living on diets deficient in fat-soluble vitamins. He pointed out that this tendency to broncho-pneumonia was independent of the condition of the bones, which is itself an indication of the vitamin D intake. For instance, when cod-liver oil was present in the diet the bones were well calcified and there was no tendency to broncho-pneumonia or atelectasis of the lungs. When butter-fat was the source of fat-soluble vitamin, the bones under certain experimental conditions were soft and portions of the lungs were often in a collapsed state, probably because of muscular paresis, but there was no broncho-pneumonia or other infective condition. When olive oil replaced butter, badly calcified bones, collapse of portions of the lungs, and broncho-pneumonia were commonly found. These results suggested that protection against infection of the respiratory tract was conferred by vitamin A and not by vitamin D.

Linked up with the problem of xerophthalmia and other infective conditions is that of the changes in epithelium induced by diets deficient in vitamin A. The first to draw attention to these epithelial changes was Mori[8] in 1922, who described them in the larynx, trachea, and ducts of many glands, including the Meibomian, submaxillary, sublingual, and parotid glands of rats. Xerophthalmia he regarded as being due to the drying of the epithelium resulting from the suppression of activity of the lacrymal glands. Wolbach and Howe[9] extended this work of Mori's