NERVE AND CORD DEGENERATION REFERABLE TO VITAMIN-A DEFICIENCY

By LUCIUS NICHOLLS, M.D., B.C., B.A. (Cantab.)
Bacteriological Institute, Colombo, Ceylon

In 1933 I inspected a large number of prisoners in the jails of Ceylon for signs and symptoms of nutritional deficiencies. The results were reported in this journal (Nicholls, 1933). The conditions which were attributed to vitamin-A deficiency were :—a papular dry skin eruption (phrynoderma), night blindness, dimness of sight, xerophthalmia, keratomalacia, a lowered resistance to dysentery, and neuritis. The last was so common that a diagnosis of neuritis had been made during 1932 in the case of 41 patients admitted to the Colombo Prison Hospital, and 2,397 treated at the dispensary. At that time the diagnosis was accepted, but at a later date more careful clinical investigations made this doubtful. There was considerable uniformity in the symptoms in the early stages, the patients complained of a burning sensation of the hands and sometimes of the feet, and numbness, tingling and weakness of the limbs. Many patients had pain when the muscles of the calves were squeezed. The reflex responses varied and were increased, normal or diminished. When the patients were placed on an improved diet recovery soon took place. A few patients developed what appeared to be a more advanced stage of the condition; and in these the clinical signs were so variable as to be bewildering, and when experienced physicians examined these patients they hesitated to make definite diagnoses and offered tentative suggestions such as :—progressive muscular atrophy of unusual distribution, ' neuritis ', ' beri-beri ', early ' tabes dorsalis ' and ' a lesion of the pyramidal tract is suggested '. Most of the patients in the later stages recovered slowly in hospital. Therefore either the prisoners, the majority of whom were young men, were at that time particularly liable to paretic disorders from a variety of causes or one type of cause was producing a variety of paretic signs.

(*Continued from previous page*)

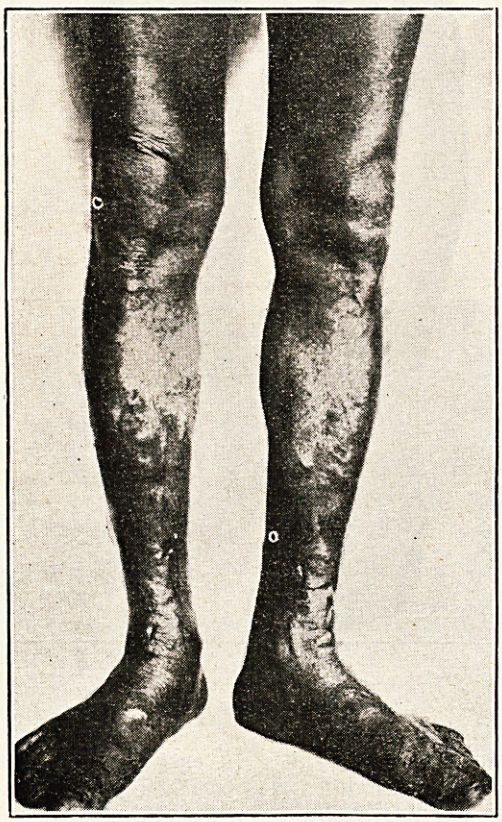

Fig. 8*b*.—After treatment.

References

Napier, L. E., and Das Gupta, C. R. (1930). A Clinical Study of Post-Kala-Azar Dermal Leishmaniasis. *Indian Med. Gaz.*, Vol. LXV, p. 249.

Napier, L. E., and Das Gupta, C. R. (1934). Further Clinical Observations on Post-Kala-Azar Dermal Leishmaniasis. *Ibid.*, Vol. LXIX, p. 121.

Signs of degeneration of nerve tissue in women in the later stages of pregnancy and during lactation have been recognized for many years in Ceylon as being far from a rare occurrence.

The early symptoms in these cases are similar to those described above for the prisoners, they start with burning sensations in the palms of the hands and sometimes also in the soles of the feet, there is tingling, numbness and muscular weakness of the limbs. Many patients do not have signs other than these, others develop mild degrees of paresis and ataxia. The great majority of the patients recover soon after childbirth. Occasionally the condition becomes worse during lactation and results in much paresis and ataxia. A few of these advanced cases are to be seen in the wards of the General Hospital in Colombo.

I selected two cases in the medical wards in the charge of Dr. P. B. Fernando, and he supplied extensive notes on them and has kindly given me permission to publish these. One case will be sufficient as it is typical of many, though not of all.

Notes on a case of paresis and ataxia of pregnancy

S. H., age 33, wife of a petty trader. Admitted on 7th March, 1935, when she was unable to walk and had loss of power in the arms and legs.

History.—Two and a half months prior to admission her sixth child was born; it was a normal delivery. Two months before the confinement she noticed numbness and tingling of both feet and hands. Gradually the numbness and tingling spread to the arms and legs. The condition became steadily worse after childbirth, and three weeks prior to admission to hospital she was unable to walk or even stand, and she could not work with her hands owing to loss of power and ataxic movements.

Plate XIII

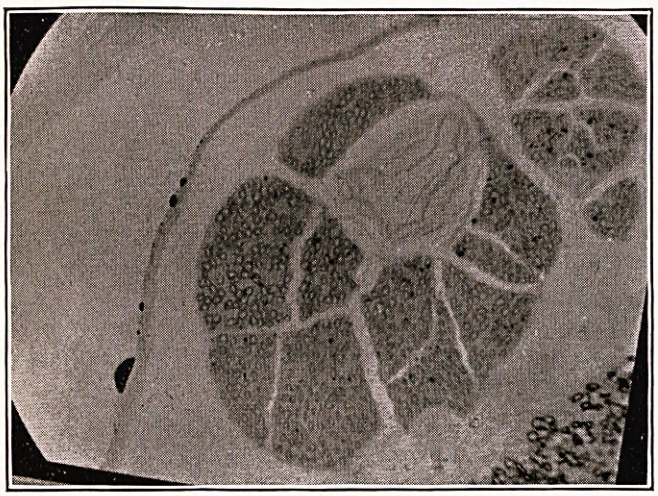

Fig. 1.

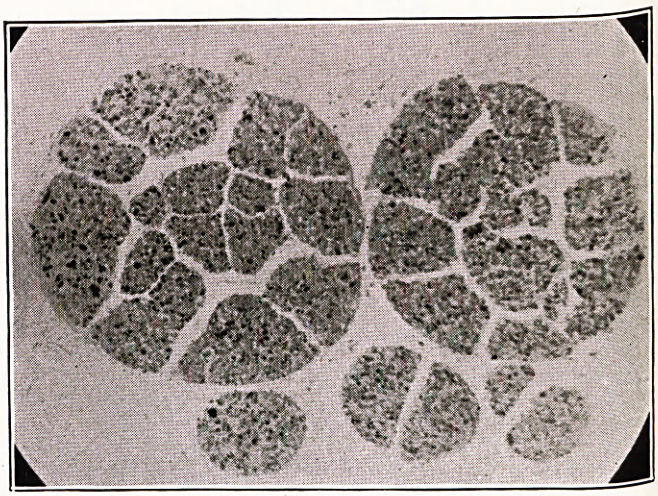

Fig. 3.

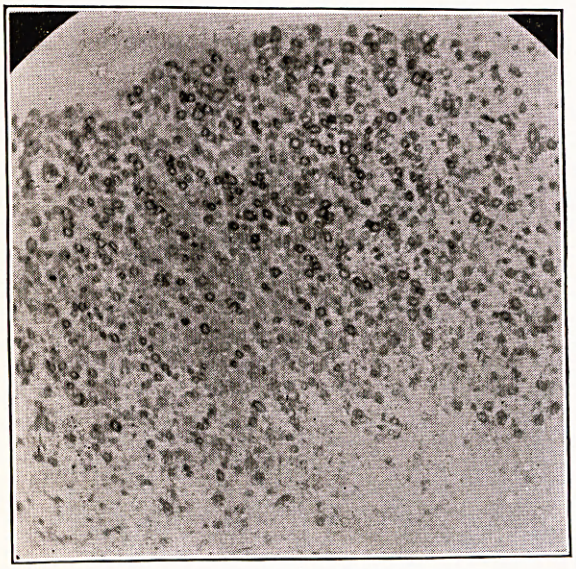

Fig. 2.

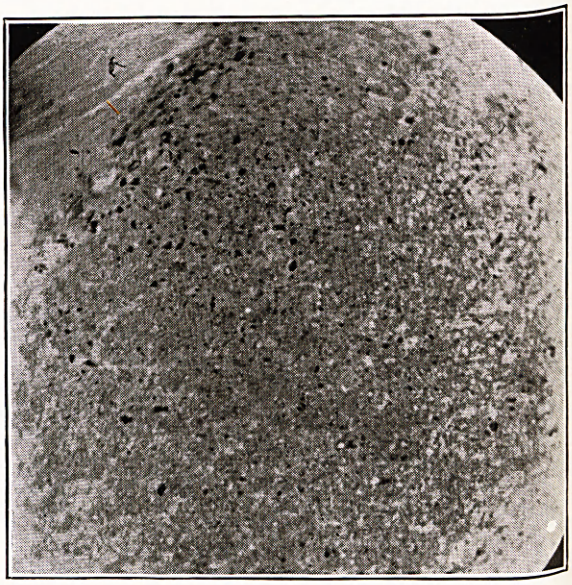

Fig. 4.

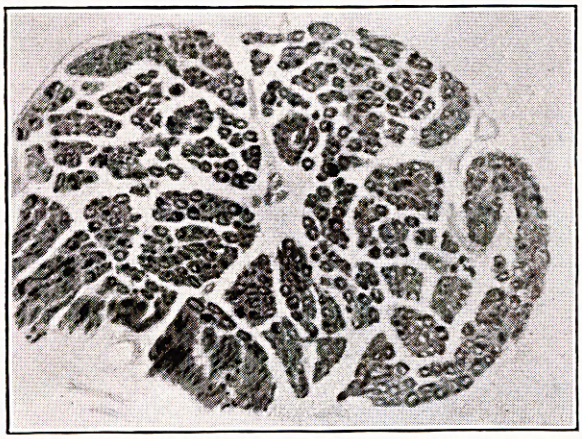

Fig. 5.

There was no history of venereal disease. She had had malaria and continued fever two years ago. Three of her six children have died, two of convulsions and one of typhoid fever.

Diet.—Her usual diet consisted of rice, vegetables, and fish. She took very small quantities of milk (just enough to flavour the tea). She stated that she never took meat, eggs, butter or ghee. For several months prior to the onset of the numbness she had been off food owing to the vomiting of pregnancy and was nearly starving herself. (There was no history pointing to lathyrism; lathyrus peas are not eaten in Ceylon.)

Clinical examination.—The patient appears well developed, there is no wasting, she had fever of 101°F. on admission. Rather anæmic.

Heart.—Limits normal. Hæmic murmur over the base. Pulse volume fair.

Lungs.—Nothing abnormal.

Abdomen.—Spleen enlarged, liver enlarged, bowels regular.

Urine.—Specific gravity—1020; albumin and sugar—nil; deposit—pus cells (about 6 to a field) and uric acid crystals.

Fæces.—Ascaris, necator and trichuris ova present.

Blood.—Malarial parasites not found. Wassermann test negative. Erythrocytes 3,760,000 per c.mm. (on 8th April, 1935); reticulocytes 1.5 per cent, average size of red blood corpuscles 7.6μ, leucocytes 5,800 (58 per cent polymorphonuclears and 42 per cent lymphocytes). Hæmoglobin 75 per cent.

Mentality.—The patient is intelligent, she is not emotional and her speech is normal.

Cranial nerves.—All normal. Pupils react to light and accommodation; no nystagmus.

Motor system.—There is no wasting of the muscles. There is marked weakness of the arms and legs. Patient can raise the legs from the bed, but not against light pressure; her finger grip is weak; flexion and extension of the arms against pressure is very weak. Wrist drop and foot drop are present on both sides. The patient cannot stand or walk.

Sensory.—There was impairment of touch and discrimination of heat and cold over the dorsum of the feet and extending up to a little below the knees on the antero-internal aspect of the legs. Pin-pricks could be felt all over the limbs. The joint sense was lost, the patient being unable to state correctly which way the toe was bent. Romberg's sign was present.

Inco-ordination.—There was inco-ordination of movements of both arms, more marked on the left side as shown by the finger to nose test. There were coarse tremors of the hands and forearms as she attempted to use them.

Reflexes.—(*a*) Superficial:—
(1) conjunctival, present and equal.
(2) corneal, " " "
(3) abdominal, " " "
(4) plantar, flexor response.

(*b*) Deep:—
(1) knee, absent.
(2) ankle, "
(3) biceps, "
(4) triceps, "

Sphincter action was normal.

Cerebro-spinal fluid.—This was clear and was not under tension. Cells were not increased, sugar 56 mgm. per cent, chlorides 700 mgm. per cent. Proteins gave Nonne-Apelt—negative and Pandy's—weak positive. Lange's curve 00000012210.

Treatment.—The patient was given cod-liver oil, and an iron mixture three times daily and marmite daily. Electrical treatment of the muscles was started on 22nd March.

In April the patient was given treatment for hook-worm infection.

Progress.—The condition of the patient slowly improved and on 10th May two months after admission the notes state 'Patient very much improved. Can walk about without assistance, muscle tone good, inco-ordination and ataxia much less, but still present. Romberg's sign is still present. Superficial sensations—touch (cotton-wool) absent over dorsum of feet, but present over the rest of the legs. Heat and cold sensations have likewise returned over the legs but are still absent over the dorsum of the feet'.

Post-mortem material

The next necessary step was to obtain material for microscopical examination. But it became apparent that many years might elapse before post-mortems could be obtained on an adult, because the mortality rate among these patients is exceedingly low, and post-mortems are not easily obtained in Ceylon.

E. Mellanby (1926 and 1934) has shown that when young dogs were fed on diets deficient in fat-soluble vitamins they develop inco-ordination of movements, and when sections of their cords are stained by Marchi's osmic acid method varying degrees of demyelination of the nerve fibres are revealed.

The death rate among young children of the lower classes in Ceylon is high and malnutrition, marasmus and debility are the causes of death which are returned for many of these.

Signs of vitamin-A deficiency such as keratomalacia and phrynoderma are common in these marasmic children (Nicholls, 1934). A clinical examination for signs and symptoms of nerve degeneration in these children was carried out and found to present great difficulties, because these children are very irritable and any handling produces crying and writhing, and this is increased when the muscles of the calves are gently squeezed, so that there is little doubt that this causes pain; but satisfactory examinations for reflex responses could not be made, even in cases where there was advanced weakness and atrophy of the muscles.

A considerable number of post-mortems have been obtained on young children, and eight of these children had shown signs of vitamin-A deficiency during life.

Pending the permission of the parents for the post-mortem it was necessary to prevent changes in the cords, and therefore 50 c.cm. of 10 per cent formalin in normal saline was injected intrathecally into each child. This was done in the first cases, but later with the assistance of Dr. O. C. Hill (Professor of Anatomy) the whole body of each child was injected through the femoral artery. These procedures were found to preserve the cords in good condition. The assistance of Dr. E. K. Wolff (Professor of Pathology) was obtained for the preparation of many of the sections. Marchi's osmic acid method was used for all the sections.

A post-mortem was made on a child aged 2 years, who had a history and showed signs of malnutrition and had died of a terminal broncho-pneumonia.

A piece of the spinal cord was removed with the posterior and anterior roots attached, sections were cut and stained; figure 1 (plate XIII)

is taken from a section of the posterior nerve roots; it shows a few degenerated nerve fibres especially in the upper right-hand quadrant of the photograph. A section of the cord of this child was searched but markedly degenerated nerve fibres were not found; figure 2 (plate XIII) is from the posterior columns. These serve as a contrast for sections (which were prepared at the same time) of nerve roots and cords, which showed much more advanced nerve fibre degeneration.

A post-mortem examination was done on the body of a child aged 2½; the cause of its death had been returned as marasmus. The body was emaciated, there was phrynoderma of the skin, and early signs of keratomalacia. The heart and lungs showed no signs of disease; the liver, spleen, kidneys and intestines were more or less normal, and the examination did not reveal any definite cause of death. Sections of the posterior nerve roots showed numerous nerve fibres in various stages of degeneration; and sections of the cord showed many degenerated fibres. The degeneration was most marked in the posterior columns but was not confined to them, degenerated fibres were seen to be scattered throughout the lateral and anterior columns. The anterior roots also showed some degenerated fibres. Figures 3 and 4 (plate XIII) are from the posterior roots and the posterior columns, respectively.

The posterior nerve roots and posterior columns of the cords of all children who had shown signs that were attributed to vitamin-A deficiency had degeneration of about the same degree as that shown in plate XIII, figures 2 and 4. And also in all cases the anterior roots and the lateral and anterior columns showed degenerated fibres.

But two children who had not shown during life any definite signs of vitamin-A deficiency, though it does not follow that they were not suffering from this deficiency, had a fair degree of degeneration of the nerve roots and cords. One of these had been diagnosed in life as suffering from malnutrition and had died with a terminal diarrhœa. The other had 'nutritional œdema'; figure 5 (plate XIII) is from a section of the posterior nerve root of the latter.

Discussions.—Mellanby has fairly definitely established the fact that some amount of the fat-soluble vitamins is necessary in the diets of dogs for the health of their nervous systems. The poorest classes of the teeming East live on diets which are definitely deficient in vitamin A, and when greater strains are thrown upon the metabolism as when women are pregnant, prisoners are placed on penal diets, and children are weaned on cereals and a few coarse vegetables, signs and symptoms of degeneration of the nervous system are to be expected among them.

It is seldom that a mean diet is deficient in only one food factor; but in primary ætiological enquiries it is necessary to dwell largely upon the most salient deficiency and, although it is suggested that vitamin-A deficiency is the cause of the symptoms, signs and microscopical appearances of nerve fibre degeneration described here, it is not suggested that other deficiencies or even neurotoxins may not play a part in some cases.

It is widely accepted that a deficiency of vitamin B_1 is the main ætiological factor in beri-beri; but most observers consider that other factors such as neurotoxins or other dietary defects may have an ancillary or even determinative action. Mellanby (1934) considers that although a deficiency of vitamin B plays an important part in the ætiology of beri-beri yet it is a deficiency of vitamin A which causes the polyneuritis. A point in favour of this is that outbreaks of beri-beri are particularly liable to occur among gangs of labourers and others who cannot afford comestibles of animal origin rich in vitamin A, and they are usually away from access to fresh garden produce. But beri-beri, showing the usually accepted signs and symptoms, is very uncommon in Ceylon, where vitamin-A deficiency is rife.

It may be that beri-beri and such conditions as the paresis and ataxia of pregnancy are closely allied and the signs, symptoms and distribution of the nerve fibre lesions are determined by the relative deficiencies of vitamins A and B_1 (and perhaps others) in the diets; in which case they fall into a natural group characterized by more or less subacute combined degeneration in which complete regeneration may take place.

The lack of uniformity of the symptoms and signs among the prisoners was doubtless due to different nerves and columns of the cords being affected to varying degrees.

References

Mellanby, E. (1926). *Journ. Physiol.*, Vol. LXI (*Proc.*, p. xxiv).

Mellanby, E. (1934). *Nutrition and Disease.* Oliver and Boyd, Edinburgh.

Nicholls, L. (1933). *Indian Med. Gaz.*, Vol. LXVIII, p. 681.

Nicholls, L. (1934). *Ibid.*, Vol. LXIX, pp. 241 and 476.

DESCRIPTION OF PLATE XIII

Fig. 1.—A section from the posterior nerve roots, showing a few degenerated nerve fibres, especially in the upper right quadrant of the photograph; from a child, aged 2 years, dying with evidence of malnutrition.

Fig. 2.—A section from the posterior columns showing slight evidence of nerve-fibre degeneration; the section provides a contrast to figure 4.

Fig. 3.—A section from the posterior nerve roots showing numerous nerve fibres in various stages of degeneration; from a child, aged 2½ years, dying from marasmus, showing clinical evidence of vitamin-A deficiency.

Fig. 4.—A section from the posterior columns showing many degenerated nerve fibres; from the same child as figure 3.

Fig. 5.—A section of a posterior root of a child who had 'nutritional œdema' before death.