of uterine atony associated with diabetes insipidus can best be performed by use of the purified oxytocic fraction.

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DISORDERS OF THE NERVOUS SYSTEM DUE TO MALNUTRITION*

BY

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Considerable and new interest has been aroused in nutritional disorders of the nervous system as a result of their high incidence among prisoners of war in the Near and Far East. These disorders have of course been recognized for a long time by those familiar with deficiency diseases occurring among more primitive peoples. My own observations began nearly forty years ago.

Three Important Points

If series of these cases showing symptoms of nervous disorder be observed, it becomes apparent that there may be a disturbance in each and every sensory function of the body without the motor system being involved. This is the first point of importance. Thus it is possible to distinguish syndromes correlated with the functions of vision, hearing, taste, and smell, with joint, muscle, positional, and vibration sense, with temperature sense, and with tactile sensibility. This group of syndromes, like all symptom-complexes, may be more or less complete or incomplete in any individual. The factors which determine their several incidences are not known; it is not known why some individuals develop symptoms and others under the same conditions manifest none.

The second point of importance is the fact that if the symptoms, more especially the early symptoms, in each syndrome be studied they will be found to be of the same order; they are homologous, though naturally they differ according to the sensory function under consideration. These symptoms consist of disorders of perception, with what might be called distortion. Though they may be of short duration pointing to a lesion which is reversible, there is a tendency towards complete failure of function.

In each syndrome—whether the disturbance be of the visual, auditory, or tactile function, for example—there may be noted considerable variations in rate of onset and rate of progress, in intensity, in intermission and remission, and in the final stage reached.

The patient who later develops amblyopia with a persisting central scotoma may complain of loss of vision for short periods lasting from a few minutes to half an hour; objects may come into focus and then disappear again; some part of an object may seem to be missing; print appears blurred as if seen through a curtain; there is difficulty in recognizing persons and objects; complaint is made of shimmering and spots before the eyes, of flickering of images, and of rings and haloes about lights, reminiscent of migraine.

The otoneurological manifestations are of similar character though often dismissed by observers with a reference to loss of acuity of hearing. There may, however, be loss of tonal differentiation: the patient can no longer understand wireless music; he may fail to understand the human voice against a background of other sounds.

Tinnitus and vertigo are common; dizziness may come on in attacks lasting a few minutes to several days and may or may not be accompanied by nausea, vomiting, tinnitus, and headache. Vestibular hyperexcitability may be demonstrated in a large proportion of cases, as noted by De Raadt, the only observer to investigate the otoneurological syndrome fully. He points out that, though this and other symptoms may be of peripheral origin in initial stages, they are essentially central symptoms.

Thirdly, consider the disturbances of tactile and pain sensibility: the patient may complain of all manner of paraesthesiae or dysaesthesiae—pins-and-needles, tingling, pricking, formication, aching, burning or shooting pains, a sensation of wetness—there may be hyperaesthesia to touch and pin-prick, followed by numbness, hypoaesthesia, or anaesthesia, characteristically patchy in distribution, incomplete, and changeable. This intermittency and variability is equally characteristic of the ataxia, hypotonia, incoordination, and Rombergism at the onset, though of course there are no accompanying subjective symptoms. To this group of syndromes must also be added mental apathy, mild depression, loss of memory, loss of emotional control, and mental deterioration.

The character of the symptoms in this group of syndromes seems to suggest a widespread disturbance of function in the cortex, both cerebral and cerebellar, and probably in subcortical nuclei. The disturbance at the onset is variable and intermittent, therefore the cause must be reversible, a fact which, it is again suggested, could be explained only by some disorder of metabolism, a disorder of the vascular system, or both.

Dietary Deficiency

That this group of syndromes is associated with malnutrition there can be no doubt. So-called toxic agents can be ruled out, though the possible action of an antivitamin must not be lost sight of. Epidemiological studies show that the prevailing dietary deficiency in all cases is one of protein and the B group vitamins, with a relative excess of carbohydrate.

Without going into details it is possible to exclude vitamins A and C as the factors in causation. Similarly thiamin and nicotinic acid may be disregarded, for though these syndromes may be present in the subjects of beriberi and pellagra they are not due to deficiency of either of these vitamins. There remain the other members of the vitamin B₂ complex to be considered. The association of these syndromes with signs of riboflavin deficiency is very

*A short communication read at a discussion in the Neurological Section of the International Conference of Physicians.

close and, it is suggested, significant; pantothenic acid and pyridoxin, closely correlated with riboflavin, might also be implicated, but for the purposes of my argument I am going to assume for the moment that a riboflavin deficiency is the cause of the condition under consideration.

The brain derives its energy solely by the metabolism of glucose. It is suggested that the initial biochemical lesion consists in a partial failure of glucose breakdown at the link between the anaerobic dehydrogenase system and the aerobic cytochrome/cytochrome oxidase system which is formed by an enzyme into which riboflavin enters as co-enzyme. In other words, there is produced a condition of anoxia or hypoxia. This of course is generalized, but only those nervous elements with a high metabolic rate, and therefore the more vulnerable, suffer as a result of this partial oxygen deprivation.

If this assumption be correct it becomes at once apparent why only the sensory side of the central nervous system is affected, for it has been shown that the oxygen consumption of the sensory nuclei is far greater than that of the motor nuclei.

The researches of Gasser (1937), Dunning and Wolff (1937), and Craigie (1939) have demonstrated, in animals, that the oxygen consumption of the grey matter of the central nervous system is very much greater than that of the white matter, that the blood supply—i.e., the number of capillaries present ("capillarity")—is proportional, but that the oxygen consumption of the grey matter is not due to the richness in cellular elements but to the neuropile (Gasser uses the word "neurophil") or mass of fine protoplasmic strands contributed by dendrites, terminal axon arborizations, and other synaptic structures.

Those areas with a high degree of capillarity and high metabolic rate include the cochlear and vestibular nuclei, Deiters's nucleus, the granular layer of the cerebellar cortex, the second layer of the occipital cortex, followed in descending order by parietal, temporal, pre-central, and insular cortices.

Conclusion

Briefly these are the arguments put forward in support of a thesis which suggests that the group of syndromes under consideration are due to failure in the metabolism of glucose in the neuropile of those areas of the central nervous system which have a high metabolic rate, in turn caused by hypoxia induced by hyporiboflavinosis and/or a deficiency of other closely associated members of the vitamin B₆ complex.

There is also some evidence that a disorder of the capillary bed (capillary dysergia) is caused by a deficiency of riboflavin coincident with the affection of the nervous tissue.

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The Minister of Health states that the following agreement has been reached between representatives of the British Medical Association, of the Associations of Local Authorities, and of the London County Council: "That for the period from July 1, 1947, until the appointed day for the purposes of the National Health Service Act, 1946, or, if new scales have not then been agreed, until the date of operation of any new scales, whichever be the later, there should be substituted for the percentages mentioned in paragraph 1 of the Interim Revision of the Askwith Memorandum agreed to at the conference held at the Ministry of Health on March 26, 1946—viz., 30, 20, and 10 respectively—the percentages of 35, 30, and 25 respectively, this substitution to include the substitution of 25% for 10% in the last line of subparagraph 1 (a)."

The Minister understands that this modification has been accepted by all parties to the Askwith agreement, and it is being circulated to local authorities by the Minister at their request.

AN IMPROVED DIRECT COAGULASE TEST FOR THE RAPID DETECTION OF STAPHYLOCOCCUS AUREUS

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As a preliminary to penicillin therapy a method has been suggested for the rapid detection of *Staphylococcus aureus* (*pyogenes*) which consists in adding the material to be investigated (pus or fluid squeezed from a swab) direct to citrated or oxalated plasma (Lominski and Grossfeld, 1944). Coagulation of the plasma indicates the presence of the organism. Positive reactions develop at 37° C. within several hours (occasionally in 20 minutes), thus being available before the results of cultures; they may also be obtained where staphylococci are too scanty to be detected in smears of the material. The reliability of the test was controlled both by culture and by the coagulase test carried out with the isolated strain. However, in the course of extended routine observations doubt arose regarding the advisability of the use of citrated plasma for coagulase tests in general, since it was found that such plasma may be clotted under certain conditions by organisms other than staphylococci. The use of heparinated plasma, on the other hand, was found to exclude this fallacy. (A detailed account of the mechanism involved, which is entirely different from that of staphylococcal coagulase, will be published elsewhere by E. M. Harper and N. S. Conway.)

Accordingly, the original method has been modified as follows: to 1 volume of citrated plasma are added 3 volumes of saline, 1 volume of meat extract broth, and heparin in such amount that 1 ml. of the mixture contains 2 to 5 Toronto units. Heparin serves the purpose of assuring the specificity of the test, while the addition of broth provides better growth conditions for staphylococci. Excess of broth must be avoided, as it favours rapid liquefaction of the coagulum and thus makes the test difficult to read overnight.

The modified direct coagulase test here described has so far proved very sensitive and highly specific, and its diagnostic value equals that of the ordinary coagulase test carried out with pure strains of staphylococci. Thus, over the last three years the reliability of this modified test has been confirmed in several thousand cases controlled by culture and the ordinary coagulase reaction with the pure strain. Where *Staphylococcus aureus* was present the results were positive in almost 95% of cases; in no instance was a fallacious positive result obtained in the absence of the organism.

The presence of other organisms does not, as a rule, prevent a positive reaction, but early reading of the test is essential, since a coagulum which forms within several hours may liquefy later owing to the presence of proteolytic bacteria. It should be added that the final test with a pure strain of staphylococcus-like Gram-positive cocci ought also to be carried out in heparinated plasma.

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