PELLAGRA

IN THE

OTO-NEUROLOGY AND RHINO-LARYNGOLOGY

BY

OTTO L. E. DE RAADT M.D.

UNIVERSITAIRE PERS LEIDEN

Erratum:

page 106 3rd line from bottom: for *signs* read: *labyrinths*

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With the publication of this work I wish to express my indebtedness *to all the medical officer colleagues* during the Japanese captivity, who by their painstaking care and cooperation enabled us to make this investigation as complete as possible.

In the P.O.W. camp Bandoeng:

To Dr Schwartz M.D. who carried out the ophthalmological examination on my cases and many others.

To my friend Dr Smitskamp, and *Dr Jenner M.D.,* who performed the general medical examinations.

To Dr Buitelaar, prewar psychiatrist to the Buitenzorg Asylum, drowned off Padang, Sumatra, in a Japanese prison ship which was torpedoed; and *Dr Van der Hoeven,* who died in a Singapore P.O.W. camp; both of whom carefully carried out neurological examinations.

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In the Cycle camp, Batavia:

To my friend Dr Bruining, prewar chief of the E.N.T. Department of the Batavia Military Hospital, with whom I worked in this camp. He also examined some of my Bandoeng cases, he being interned at Tjimahi at that time.

To my friend Dr Verhaart M.D. neurologist to the University of Batavia who coexamined many patients with Dr Bruining and myself.

In Pakan Baroe camp 2:

To Dr Verhaart who examined many cases neurologically and whose examination of brains obtained post mortem was of inestimable value.

To my friend the lieutenant colonel L. Simons M.D., Royal Dutch East Indies Army Medical Corps, who performed

post mortem examinations without gloves, with improvised instruments, and under other most adverse conditions.

To my friend the lieutenant commander Van Swelm, Royal Dutch Navy Medical Service, for his rare genius for finding and manufacturing food and yeast for the community; who taught and showed us the tremendous importance of collective measures concerning food and hygiene.

To my friend the interpreter Kraal to whose untiring efforts is due the credit for securing many important concessions for both sick and other prisoners in the Pakan Baroe camp.

To all, who brought scientific interest and a little happiness into this dark period, I cannot sufficiently express my warm appreciation.

Further my acknowledgement is due to the following:

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And lastly *to my mother*, to whom I owe so much and who willingly gave me much technical aid and encouragement in the writing of this book.

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„Candida", Oegstgeest (Holland)

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CHAPTER I. INTRODUCTION

In March 1942 the Japanese Air Force, Navy and Army made their final advance in the South West Pacific, the isle of Java being one of their last conquests. Many allied soldiers were captured there and gathered in several camps. After shuffling them about for some months the Japanese in October 1942 started forming working parties ranging from 500 to 3000 prisoners of war for several territories, stretching from Sumatra, Burma, Thailand and Japan in the West and North to the Spice Islands and Timor in the South-East. Many prisoners died in those working-camps, mortality ranging from 10 % on the island of Flores to 90 % in some camps working on the notorious Burma-Thailand railroad, where cholera appeared. Moreover several Japanese prison ships were torpedoed with considerable loss of life.

The food supplied to the prisoners of war (P.O.W.s) was qualitatively deficient from the start; in addition in the later stages of captivity the number of calories was definitely insufficient. This varied from 1500 to 2500, being below 2000 most of the time in the later stages. Further, as soon as a P.O.W. was no longer able to work, about 700 calories were withdrawn in the form of rice. With regard to the quality of the food, highly polished and old rice *) formed the staple

*) Rice (Malay: *paddi*), when harvested and thrashed (Malay: *gabbah*), has to be unhusked (Malay: *bras*) before being boiled and eaten (Malay: *nassi*). The unhusked grain of rice is enveloped in a pericarp and aleurone layer, while at one end the germ is lying under the pericarp (M a n s o n B a h r [74]). These layers (Dutch: *silvervlies*), also called *silverskin*, contain salts (e. g. phosphor), fat, protein and the B vitamin complex in considerable quantities, while the grain as such contains practically no vitamins and fat, but some protein, thus consisting mainly of carbohydrate. For storing rice (bras) away for a longer time, removal of the silverskin is desirable, because otherwise the rice will become musty. To this end the rice is milled and polished, in which process highly valuable dietary components are removed with the silverskin and germ. The removed particles form

diet in the most favourable case. In many camps, notably outside Java, a considerable part of the rice was replaced by cassave-flour, which is nearly pure carbohydrate, from which all the water soluble vitamins are washed away in the process of fabrication. This means the whole vitamin B complex and vitamin C. Vegetables were scanty, meat very little was available in the Java camps and practically absent on the other islands. In Pakan Baroe the average was a few grams animal protein per man per day. Our biggest source of protein was the rice, thence the catastrophic results when part of it was replaced by cassave flour. Moreover, this was only vegetable protein. Fat amounted in the camps outside Java to a few grams per man per day; in Java there was slightly more. Summarizing we can say that the food consisted mainly of carbohydrate, little protein and less fat, was inadequate in vitamins, and often deficient in caloric value as well.

In every camp the Japanese guard started a racket, by which it was possible to buy small quantities of extra food, mainly for the sick. Because to some extent we could make our own choice this food was much better as to fat, protein and vitamins, but was very scarce owing to the fact that it had to be bought by our own means, and the prices in the free market soon rocketted sky-high. Moreover, the guards had to be compensated for their generous connivance.

Concerning supplies of clothing, shoes, drugs, dressings, soap, etc., the Japanese took everything and brought nothing. We had to live (and die) on those parts of our own Army stocks we had managed to save, repeatedly reduced by Japanese confiscations. It will be clear that under those circumstances we ran out of everything rather quickly. Another chief cause of serious illness and death was the pitiless squeezing out for heavy manual labour of any man able to walk, never

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a substance bearing some resemblance to fine sawdust (Malay: *dedek* or *katoel*), being mainly exported as cattlefood. It is very cheap and cattle thrives on it, small wonder. There was always abundance of this stuff in the areas we were but we could obtain it only occasionally and in small quantities, while the Japanese fed it to their pigs. They may at times have had great difficulty in obtaining vegetables, meat, fish and oil for us, but the withholding of dedek, which could have saved many lives and prevented many symptoms, was unpardonable.

granting any convalescence after an attack of malaria or dysentery, two scourges notably of the camps outside Java. It was no exception to see prisoners perform heavy labour, in whom the diagnosis beriberi or pellagra could be made from a distance.

From the abovementioned it will be clear that conditions under which most P.O.W.s lived became more and more those of starvation, filth and lack of suitable clothing. The starvation began partially, as avitaminosis, whilst the general appearance of the men might be still reasonable or even good; later it became more or less complete, covering all dietary factors.

In the camps medical teams were formed out of the prisoners, physicians and orderlies being taken prisoner as well. With regard to the physicians, these teams consisted of general practitioners and teams of specialists, as far as available. During my whole internment of 3½ years I served as Ear, Nose and Throat specialist in such a team, in three different camps.

I. Bandoeng (March 1942—December 1943)

We saw many cases of avitaminosis even as early as this. Conditions here were reasonable, although it required a stay in two other camps to realize this, everything in this world having only a relative value. The number of prisoners in this camp was on the average 6000, the number varying on account of many incoming and outgoing drafts.

Schwartz in August 1942 recognized retrobulbar neuritis to be one of the first signs of dietary deficiency. This was closely followed by scrotal dermatitis, seborrhoic eczema of nose and nasolabial folds, hyperkeratosis pilaris of the surfaces of the elbows and knees (Hurwitz†, H. Simons, dermatologists, and Van der Meer, medical officer). At the same time "burning hands and feet", cheilosis, angular stomatitis (perlèche), glossitis, stomatitis, pharyngitis, inflammation of the vestibulum nasi and laryngis were reported in "epidemics" by many doctors and classed as evidence of dietary deficiency. The classical pellagrous dermatitis we did not see until April 1943 (Hurwitz†, Van

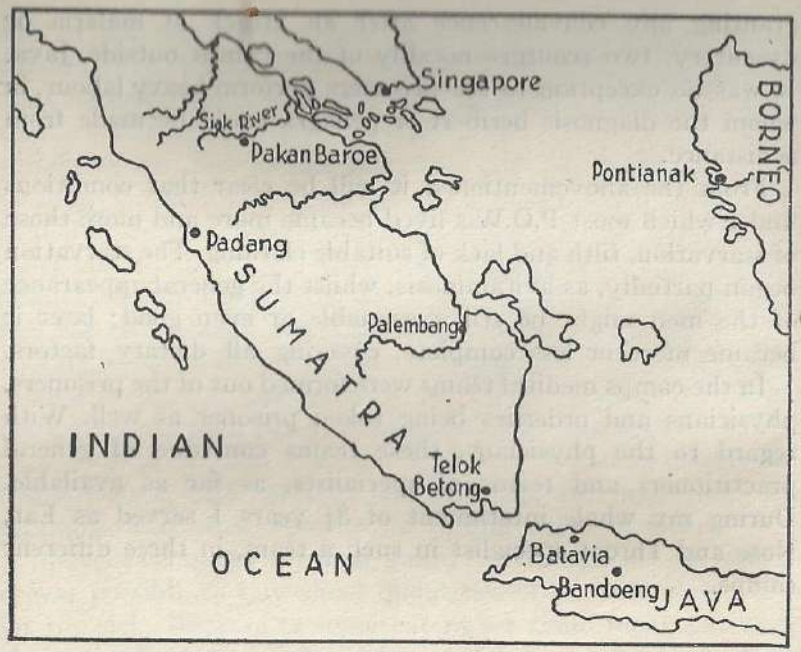


Fig. 1. Map showing Bandoeng, Batavia and Pakan Baroe. Scale 1 : 14.000.000.

der Meer, R. Simons), when a group of P.O.W.s from Sourabaia came into our camp after a period of more intensified malnutrition.

In March 1943 attention was drawn to a new symptom, dizziness. It soon became clear that this vertigo occurred in so many cases that a definite relation to the P.O.W. conditions could not be denied. On inquiry many patients stated they had felt periods of dizziness before, beginning in August and September of the previous year. Others made complaint of slight dizziness continuously for six months, but reported only because they saw that a new doctor was interested in this symptom just now. Eventually a subjective and an objective symptom complex were found, best classified as oto-neurological. This thesis reports chiefly on this syndrome.

In Bandoeng 160 patients were examined extensively, including ophthalmic (Schwartz), general (Smitskamp and Jenner), and neurological investigation

(Buitelaar† and Van der Hoeven†). Conditions here were such that a fairly thorough examination could be carried out, although many interesting and essential tests could not be done, as will be realized. Case-reports on these 160 patients were buried when the camp was dissolved in December 1943 and retrieved by Smitskamp, on the cessation of hostilities with Japan. From these records data for this thesis were obtained. Statistically, I will limit myself to this group of patients.

On the dissolution of this camp the internees were brought to

3. **Batavia**, Cycle Camp (December 1943—May 1944)

Conditions here were much more adverse than in Bandoeng. Although I had the pleasure of working side by side with my friend Breining, we had opportunity neither to perform any more extensive examination, nor to keep any written records. Most of the time moreover was absorbed by treating commonplace ear, nose and throat affections, accommodation being very primitive and any small treatment taking much time. The same oto-neurological symptom complex was seen here as well, as was to be expected. In May 1944 I happened to be detailed with a draft proceeding to the centre of Sumatra near a small village,

4. **Pakan Baroe** (May 1944—October 1945)

We stayed here until after the Japanese capitulation, being completely bewildered within a short time by the conditions prevailing in this camp. „Abandon all hope, ye who enter here" was missing above the entrance.

In the course of time more drafts came to the Pakan Baroe area. The aim was to build a railroad crossing central Sumatra. Approximately 700 out of 5000 P.O.W.s died here, and from a rough estimate, 80.000 out of 100.000 native coolies. From these coolies we were always strictly segregated, they lived in other camps.

The Pakan Baroe period may be called a gigantic experiment in which 5000 white people, born in beds, reasonably clothed,

fed and lodged for on the average 35 years (mean age), and for the greater part not accustomed to heavy labour, were moved into a malarious and dysentery ridden country, clothed

Fig. 2. The notorious railroad. Cost approximately one human life to every third sleeper. Drawn by H. Menne.

and fed shamefully, living in leaf huts with earth floors (if they were lucky), building a railroad through marshes and jungle with very few drugs and other medical supplies at their disposal. Till February 1945 there was still some quinine, after that date we had to take pulverised Peruvian bark when

we got malaria. On this powder many patients reacted with diarrhea, which meant death for a certain percentage. With the minimum of food on which we had to live diarrhea meant overt avitaminosis or death. Normal bowel function was the most important matter, as with infants. Instead of "How are you?" men (notably physicians) greeted each other with: "How are your motions?", a joke, eerie in its truth.

Fig. 3. One of the four „hospital" huts. Drawn by F. de Jong.

Pellagra with its uncontrollable diarrhea, beriberi, malaria, bacillary dysentery and tropical ulcers of enormous size killed most of those 700. Pellagrous dermatitis, famine oedema and extreme emaciation were quite common occurrences in this camp.

They died completely wasted or shapelessly distended with anasarca and serous effusions; always paralytic, helpless and bedridden; often covered with bedsores, an excellent soil for larvae of bluebottles. Strange to say, on the one hand there was often complete insight into the situation weeks and hours before death, they might discuss it and put their affairs right in an almost intelligent manner. Several times one could talk

to a man with absolutely unclouded consciousness, who died within half an hour. On the other hand there were many who became delirious, a certain sign of impending coma and death.

I feel this is the place to express my profound admiration for warrant officer Van den Berg and his corps of orderlies. They toiled on amidst filth and horrors, with little soap and no disinfectants, repeatedly stricken by malaria and

Fig. 4. The post mortem locality. Two are wrapped up in a „tiker", a sort of native covering for floors, plaited from leaves. Dr L. Simons is performing the post mortem. Drawn by F. de Jong.

dysentery, hypovitaminotic, many developing oedema. They collapsed practically *in toto* none to early, when evacuation of the sick had taken place; after carrying on in the last months by sheer willpower to finish their task. I remember quite clearly the shock allied Army doctors got on coming into our camp-hospital after being parachuted in after the cessation of hostilities.

The same oto-neurological syndrome, referred to above, was seen frequently. Examination could be done only superficially. Records on these patients were kept, but unfortunately lost.

On the other hand after many difficulties we could do some 30 post mortem examinations (L. Simons and Verhaart), but only macroscopically. There is still a chance left that microscopical examination of some secured specimens of brains can be performed later.

Roughly estimated, a few hundred patients with the oto-neurological syndrome were seen in Batavia and Pakan Baroe. Moreover some of my Bandoeng patients could be followed up during the whole captivity.

Summary

Japanese captivity for me consisted of three periods:

1. Bandoeng (March 1942—December 1943); 160 patients with an oto-neurological syndrome were examined rather extensively. Conditions were reasonable. Records available.
2. Batavia (December 1943—May 1944), conditions bad.
3. Pakan Baroe (May 1944—October 1945), conditions indescribable. In Batavia and Pakan Baroe a few hundred more patients showing this syndrome were observed, no records available. About 30 post-mortems were performed, macroscopically only.

Statistics will be confined to the Bandoeng group of 160 patients.

CHAPTER II. SYMPTOMATOLOGY

In the set of symptoms now to be described, the vertigo which gave rise to this investigation, proved not always to be present.

A. SUBJECTIVE SYMPTOMS

1. Dizziness

By dizziness or vertigo is meant a sensation of movement of the surrounding in regard to the body, or of the body in respect to the surroundings, while this movement in reality is not present. Leidler [68] will add to this the accompanying disturbance of affect, which mostly is disagreeable, but may be pleasant, notably in neurotics. In our patients the sensation was always unpleasant, ranging from minor degrees to feeling exceedingly ill and anxious.

This dizziness might have the character of a *typical rotatory labyrinthine vertigo* (39 cases). In such cases it came on in attacks, lasting some minutes to some days. The intensity might vary greatly, sometimes it was so severe that the patient was unable to remain on his feet. When occurring at night, which was not rare, the patient would clutch for support in fear of falling from the bed. In several of such cases the attack was dependent upon a certain position of the head. The patient being in a lying position when the attack occurred, it is most probable that the attack was elicited by head position and not by neck reflexes. Unfortunately in such cases mostly no objective verification by observing a positional nystagmus or vertigo could be obtained in the examination, which of course took place later (record 18, 153).

Nausea, *vomiting*, *tinnitus* or *deafness* might or might not accompany the attacks. The most consistent correlating symptoms were *sweating* and *headache*. The sweating might

be so profuse that the thin tropical clothing was soaked in a few minutes. The patients mostly felt seriously ill in a severe attack, but sometimes the disturbances were limited to severe vertigo, headache and sweating, subsiding readily when the patient lay down and gave his eyes rest. In other cases the vertigo was moderate or very light, correlating symptoms like headache, sickness etc., sometimes being far worse than the dizziness (pat. no. 129).

The cases I was able to see during the attack always showed nystagmus, mostly to both sides, first degree, more marked to one side, horizontal or less frequently horizontal-rotatory.

The frequency varied from more than one attack per day to one solitary attack in the whole camp life. Between the attacks the patient was either completely free from complaints, or there remained a little dizziness in some form.

In 31 cases the sensation of movement was either *linear*, or consisting of *rotatory or linear to and fro movements*, or *obliquity of the surrounding*, or *rocking movements*, or the sensation of the foot of the bed going up and down. It might so happen that whilst walking, the inability to deviate or, conversely, the necessity to turn to the side, was experienced, a collision or a fall being the result. In other cases there was uncertainty of gait only, resulting in a quick step to the side unexpectedly. In all these cases there was a sensation of vertigo as defined above, but this mostly was of secondary importance to the loss of balance, compulsary movements, or blocking of certain movements.

Finally, 31 other cases are included here where the chief complaint was "dizziness" which on further inquiring proved to be a more or less complete *black out*. However, profuse sweating and headache were fairly consistent concomitant symptoms; many of these cases had rather vague sensations of real vertigo in the attack, such as a feeling of swaying, which did not occur in reality. This black out is a common symptom in debilitated and perhaps also in other people on rising from a crouching or lying position. In these patients, however, it occurred frequently whilst walking, lying, or otherwise. All these symptoms to me seemed to justify inclusion under the heading dizziness.

The form of dizziness might change in the course of time in one patient, sometimes several forms occurred alternatingly or simultaneously. The dizziness in all forms sometimes arose without appreciable cause, but in most cases it was evoked or increased by conjugate movements of the eyes, notably lateral gaze and convergence, much less so by upward gaze. Reading, playing chess, or lighting a cigarette in which they looked at its point, had such effect. The most fatal influence was exerted by the Japanese weaving factory, where the eyes constantly had to be fixed on moving objects, demanding a continuous alteration of direction of gaze, convergence, and accommodation. Many patients got their first attack in this factory. Quite often sudden movements of the head precipitated an attack, much less so stooping or certain positions of the head.

Nausea or vomiting and attacks of profuse sweating, mostly with, sometimes without vertigo, were reported in 62 and 47 cases respectively.

Comment

Considering the vertigo alone, its long standing and low intensity in many of the patients, who were never completely free of it, suggests a central cause rather than a peripheral one. On the other hand there were cases with clearly limited attacks of considerable severity, who were completely free between the attacks; here the dizziness had a more peripheral character (Aubry[4], Klestadt[55]).

This dizziness was reported in 101 cases out of a camp population of 6000, counting only patients in whom objective findings were to be found. As will be clear from the preceding, there might be a complete *Ménière's syndrome*; in many cases, however, only the vestibular part gave symptoms, those of the cochlear part being absent. These latter cases are more probably from central, than from peripheral origin; again, looking at the subjective symptoms only.

In the literature we find vertigo, affecting larger groups of people in two diseases:

1. *Paralysing vertigo*, or *Gerlier's disease* (Bing[13], Wechsler[142].
2. *Pellagra.*

Gerlier's disease will be discussed later, neither in Bandoeng nor in Batavia we had reason to think of it.

In every book or publication on pellagra vertigo, in some cases associated with a peculiar tendency to fall backwards, will be found in the first paragraph on the initial symptoms. Therefore I will give here a few sources only: Manson Bahr[74], Niles[85], Castellani and Chalmers[20] for tropical diseases, Bing[13], Wechsler[142] and Kinnier Wilson[54] for neurology, Bicknell and Prescott[11] for vitamins; further any publication on the symptomatology of pellagra.

Strange is the absolute absence of any report of vertigo in pellagra in the oto-rhino-laryngological bibliography at the end of this thesis. It should be borne in mind that this is an initial symptom, developing long before the disease becomes full-blown. *Formes frustes* of B complex avitaminosis are to be expected everywhere, if not frequently, certainly as isolated cases.

2. Tinnitus

This symptom was present in 56 cases. An attempt was made to differentiate between tinnitus caused by deficiency, and that resulting from another cause. In 33 of these 56 cases an obvious cause could be held responsible, like quinine medication, nicotine abuse, occupational causes, otosclerosis, middle ear affection, etc. Of course the possibility has to be borne in mind, that in these 33 cases a camp influence was acting together with one of the enumerated causes. The same line of thought was followed in considering the cause of subjective and objective hearing loss.

This tinnitus might have all degrees of intensity, a lower or higher pitch, and varied greatly in the character of the sound. Sometimes it was continuous, in other cases it came on in attacks, correlated with dizzy spells, or was completely independent thereof. It was often associated with deafness, but not necessarily so, and was nearly always bilateral. It was never as annoying as it may be in some cases of otosclerosis.

3. Subjective hearing loss

This was observed by the patients in 45 cases. In 26 of these a known cause possibly was responsible, in the same way as with tinnitus. The deafness was mostly moderate or light, and not annoying.

However, one case not being able to hear conversational voice ad concham was observed. This was a young English soldier, who entered captivity with normal hearing. A period of serious malnutrition followed: in one year he became so deaf that he started learning lip-reading and finger-alphabet. Then food conditions became better, resulting in his hearing whispered voice ad concham and conversation without much hindrance after a further year. This patient was thoroughly observed by Bruining (Tjimahi). Later he was transferred to the Bandoeng camp hospital, where I had the opportunity to examine him superficially. No written record on him was kept by me. He was one of the cases which Bruining assumed was a deafness, caused by deficiency, being the first physician in the camps to realize this.

Deafness was not always accompanied by tinnitus, neither was this by deafness. Often there was hearing loss objectively, without the patient himself being aware of this. The reverse was never observed: when the patient complained of impairment of hearing this could always be confirmed objectively.

Strange is one patient (no. 160) with objective bilateral deficiency deafness of approximately the same degree on both ears, who was aware of hearing loss and tinnitus on the left ear only.

4. Headache

This was a frequent complaint (75 patients). It often accompanied attacks of vertigo, but also occurred much more than before camp-life without dizziness. It was definitely occurring more than before captivity in 46 cases and was often provoked by convergence, lateral, or sometimes upward gaze. In general exertion of the eyes was a frequent cause, although it not infrequently occurred without appreciable cause. It might be unilateral, frontal, or vertical, much less frequently occipital. It varied from slight complaints hardly incapacitating the person, to fulminating pains, making a man weep.

Accompanying vertigo might be a severe rotatory dizzy spell; more often, however, it consisted of other, less disturbing

vertiginous sensations. Nausea, vomiting and sweating might go with the headache, notably when vertigo was present as well. Sometimes scintillating scotomas preceded the attack, in those cases there was no difference from migraine. The headache might come in attacks, lasting some hours to some days, or have a more continuous character. There were people who nearly always were bored by it, then mostly not severely.

5. Complaints on eye movements

Many patients complained of *presbyopia*, occurring too early or being too marked in respect to the age. Objectively this was confirmed by Schwartz. *Difficulty* and slight pain in the eyes in *looking laterally* (67 cases) or in *converging* (70 cases) were reported, much less so in *upward gaze*. This difficulty in looking laterally might be so pronounced that one patient said he was compelled to turn the whole head when he wished to look at an object only a little sideways, like a horse with blinkers. Nevertheless, he was able to make the conjugate lateral eye movements, but only at the expense of extremely uncomfortable sensations. All these movements favoured precipitation of headache, dizzy spells, nystagmus or all of them simultaneously.

There were frequent complaints of *diplopia*, notably after exertion of the eyes. Intelligent patients observed that it was evoked or increased by looking laterally, and, by covering one eye, that it was binocular.

6. Pick's visions

A rare and peculiar symptom, in my opinion best classified as partial visual vertigo. Whereas in vertigo the whole surrounding may seem to move, these patients see part of their visual field move in respect to the surrounding objects. Thus they see persons move through walls into another room and move about there; or walls bending and being displaced. Two of our patients spontaneously reported an experience, very strange in their (and in our) opinion. While reading, one or more letters came out of the line and stood above it,

obliquely or upside down. It was no diplopia, their original space being empty. I told the patients to give due attention hereto on recurrence of the visions. Both experienced this several times, but only temporarily. Error as to the diplopia was excluded in my opinion. Schwartz and I valued this phenomenon to be identical with Pick's visions.

Comment

This not generally known phenomenon has received little attention in the literature. In the entire bibliography at the end of this thesis only Bing and Dorland [30] mention it. According to Bing it is observed in affections of the tegmentum pontis, in the floor of the 4th ventricle, and especially in lesions of the posterior longitudinal bundle, connecting the vestibular nuclei with those of the extraocular eye muscles. These lesions may precipitate disturbances in coordination between vestibular and ophthalmostatic impulses. Mostly they are accompanied by diplopia and nystagmus [13].

7. General symptoms

Many suffered from *mental* and *physical lassitude*, although the general condition sometimes was still very, and often reasonably good. I may refer here to Dumoulin's [32] excellent article on deficiency symptoms in allied P.O.W.s in Thailand, unfortunately placed under "Feuilleton". He states: "There were frequent complaints of vertigo. To regard general weakness as the cause mostly needed no consideration, because this complaint was observed in a very early stage, long before there could be any question of decline in general condition."

Anorexia, insomnia, moroseness, lack of energy, melancholy, psychic incontinence, anxiousness were frequent complaints.

The food in general was monotonous and unappetising. Many patients spent the little money they had on sweets and other non nutritional and under our conditions even dangerous dainties. Often valuable food was discarded in Bandoeng, because it was tasteless, every day the same, people making up for the loss in calories by the purchase of

sweets, which was possible there. Of course we fought against such habits, but only with moderate results. Indeed there was a craving for any other food and taste, that can be understood only by people who lived under the same conditions.

Psychic changes were frequently observed in our cases. Therefore in the aetiology of the somatic symptoms we bore in mind the possibility that certain patients too readily gave in to lack of appetite. But it is also possible that the psychic and the somatic symptoms were of themselves part of the same clinical picture.

In some cases there was *irresistible sleepiness*. *Nausea* and *vomiting* occurred more than normally (62 cases), also without dizziness.

Periods of diarrhea with more than 5 motions a day in the history or while under observation were observed in 58 cases. Among the first group there were certainly a considerable number with bacillary dysentery, how much we can only guess. In addition there were 9 patients with periods of diarrhea with less than 5 actions per day. Sometimes these periods lasted for months, interspaced by stages of normal motions or even constipation. *Frequent micturition*, notably at night, depending partially on increased urine excretion, was a common symptom among all P.O.W.s; and in our patients also.

Ataxia, notably showing itself in the dark, was frequently experienced as extremely annoying (for incidence see objective examination). Conceivable, in view of the fact that they frequently had to rise from bed in a pitch dark camp to reach a latrine 100 and more metres away. Rising 6—8 times during one night for micturition was quite common. When diarrhea or burning hands and feet in addition drove them from their beds it can be imagined how much time remained for rest at night.

8. Other deficiency symptoms

The *"burning hands and feet"* were an important problem (101 cases). It occurred in an extremely high percentage in the rest of the camp population as well. It ranged from prickling sensations, similar to the feeling when coming from a winter

temperature into a hot room near the stove, to maddening burning, chiefly at night. Dull aching, sharp stabbing, or boring pains were also reported. Considerable numbers came out of bed at night to put their feet on the cold concrete, in the gutter or in a bucket of water to alleviate their pain by refrigeration.

Relapsing attacks of sore mouth were common. The mucous membrane of lips and tongue was irritated and very painful on contact with hot, spiced, crisp or hard food; profuse salivation annoyed the patients. *Painful swallowing* often accompanied this, less often *forming of crusts in the vestibulum of the nose*. Itching, burning and *redness of the scrotal skin* was a frequent concomitant symptom. All the complaints, enumerated in this paragraph, occurred or had been present in one or more forms in 53 cases, and were distributed as follows:

scrotal dermatitis	37 cases
perlèche	28 „
stomatitis (glossitis included)	20 „
cheilosis	11 „
pharyngitis	3 „

Sore mouth, painful swallowing and lack of appetite adversely influenced food intake. Together with the aforementioned gastrointestinal disturbances they provided ideal conditions for the establishment of a vicious circle.

Ophthalmically *blurred vision* (45 cases), *lacrimation* (8) and *photophobia* (32) were reported, also *itching and burning of the conjunctivae* (10 cases). Many patients could not come into unshaded light without dark spectacles, whereas formerly they never suffered from the tropical light.

All these symptoms were readily recognised as caused by deficiency as early as August and September 1942, although in the beginning there was disagreement as to which vitamins and other dietary factors were missing. They had a considerable higher incidence in our group of patients than in the rest of the camp population, a further indication for the aetiology of the vertigo as well.

Comment

Vertigo, headaches, mental symptoms as described under general, are frequently met initially in pellagra [20, 74, 85, 13, 142, 11] (and many other sources, for instance Frostig and Spies [39]). Digestive tract complaints, the eyes, nervous system and hearing will be discussed in the objective symptomatology. The single remark may be allowed here that Burgess [18] noted the same discrepancy between subjective complaints and objective findings in deficiency deafness in allied P.O.W.s at Changi, Singapore, in the same period.

The burning hands and feet, occurring in some 500 patients at Bandoeng and thoroughly examined there by Smitskamp, form an extremely interesting problem. Cruickshank [25] describes the symptom in allied P.O.W.s in Changi camp in the same war. He obtained the best results with di aethyl nicotinamide, intravenously, which cured or considerably relieved some 65 % (same vitamin-activity as nicotinic acid). Simpson reported the same affection in P.O.W.s in Java [113] and Harrison at Hongkong [49]. Manson Bahr describes the symptom under the heading of beriberi and again under pellagra. He is more inclined perhaps, to attribute it to ariboflavinosis or to pellagra, than to beriberi. Vedder considers it to be an early symptom in pellagra [140]. Moore, Scott, Landor and Pallister observed it in association with ataxia, weakness, loss of visual and auditory acuity [74]. Stannus considers the sign as almost pathognomonic of pellagra (Bicknell and Prescott). B_1 gives no relief, nicotinic acid alone by Kark is said to aggravate the symptom. Stannus believes riboflavin to be the responsible missing factor [11]. The same difficulty in determining the responsible factor of the B complex is always encountered (see comment on cheilosis and perlèche).

In my opinion the symptom is not sufficiently stressed in pellagra and associated deficiencies. It was one of the chief problems in our camp, having a high incidence and being extremely annoying. Smitskamp in Bandoeng tried massive doses of B_1 without much result. Nicotinic acid and

riboflavin were not available. His findings will be published shortly.

Summary

Vertigo, headaches, impairment of hearing and tinnitus, complaints on conjugate movements of the eyes and their weakness were the main subjective symptoms from an oto-neurological point of view. Other deficiency symptoms of the eyes, digestive tract, nervous system and skin were frequent. Two cases experiencing Pick's visions were observed.

B. METHOD OF EXAMINATION

Each of the 160 patients were examined by *otoscopy, anterior* and *posterior rhinoscopy*, inspection of *mouth* and *pharynx*, and *mirror laryngoscopy*.

Spontaneous nystagmus was looked for in *straight ahead gaze* and in the *four other directions of gaze*. The extreme lateral eye position was avoided, although it must be stated that most of the cases showed nystagmus only in a lateral eye position not far from the extreme. Frenzel's or Bartels' spectacles were not available, so that fixation could not be excluded. All the observations were made while fixing the top of a finger or some other object, which was moved slowly in the different directions, approximately half a meter in front of the patient's eyes.

Positional nystagmus was only looked for in some of the cases, because of lack of time and accommodation. Thus the incidence of positional nystagmus in this syndrome might be higher than was found. It was carried out in the following manner: The head was bent 1st: right ear down, 2nd: left ear down, 3rd: face down, 4th: face upwards, in the sitting patient, all movements being partially followed by the body. In every position the eyes were observed in the five directions of gaze. If there was any distinct change in a nystagmus existing in normal position, or if a nystagmus appeared, the test was repeated in the lying patient, on the right and left side, in supine and prone position, to exclude a nystagmus elicited

by neck reflexes or by vascular disturbances. Unfortunately at that time partly my knowledge on the subject, partly local conditions prohibited more exact and consistent tests, the same holding for several other parts of the examination.

It soon became clear that *weakness of lateral gaze* and of *convergence* were frequent symptoms. Thereafter these movements were always tested, in this case bringing the eyes in the extreme positions on purpose. Some time later anisocoria, form anomalies of the pupils and mydriasis were noticed; so the *pupils* were included in the examination with their reflexes as well.

For *hearing tests* there were available one tuning fork a 1, whispered and conversational voice and a space of 8 meters length, which was fairly free of extraneous sound during certain hours of the day. With this poor equipment and in view of the extreme importance of this part, great pains were taken to elaborate the *whisper test*, using many words and dividing them carefully in those consisting of *higher*, and those of *lower frequencies* in the tone range of whispered voice (Zwaardemaker and Quix[145]). Repeated check tests were taken with keen hearing young individuals as to the normal distance required for hearing my whispered voice, which was made to be only just intelligible from 6 meters distance for the lower frequencies.

When hearing was not normal, or retraction of the drumheads present, *tympanic inflation* was practised by means of a Politzer bag and nasal tip. When no distinct inflation was obtained, a tubal catheter was applied and the sound of passing air noted with the auscultation tube. The longest hearing distance obtained was taken into consideration. After inflation the influence of this procedure on a spontaneous nystagmus was checked.

The Rinne, Weber and Schwabach test were now carried out. The bone conduction was measured from the vertex when there was no considerable difference in acuity of hearing on both ears; in the other case from each mastoid separately. Here again frequent checking on young keen hearing individuals was observed to exclude hearing loss of the examiner and to make allowance for his age (36 years).

Thus by normal hearing is meant whisper distance, Rinne, Weber and Schwabach for 435 double vibrations normal.

It may be added here that Bruining at that time was interned in the Military Hospital of Tjimahi, 12 K.M. away. For several operations we were allowed to transfer patients from the Bandoeng camp to Tjimahi Hospital. Bruining, having heard of my findings, asked me to transfer some nystagmus cases to his hospital under some pretext, which was arranged. Some patients with nystagmus and normal hearing were selected and occasionally transferred, one by one. I knew he possessed a serviceable sound damped (nearly sound proof) room, a complete set of tuning forks and Struycken's[132] monochord, having worked there myself before the war for 7 years, and the room having been built according to my plans in 1937.

Now Bruining also found normal hearing in these patients with more extensive equipment, although audiometric examination was impossible. Also turning tests were carried out by him, having an otological turning chair. I do not know the results, which probably will be published in the near future.

After the hearing tests, the *Romberg test* was done in the usual manner. In case of falling dependendability upon head position was always checked.

Then the *pointing tests* followed; in the vertical plane about midway between the frontal and the sagittal one, and in the horizontal plane.

The *walking test* was carried out in the usual manner over a distance of ± 8 meters, forward, and if the patient was not too ataxic, backwards as well.

Caloric vestibular irritation followed, done in Atkinson's method [8], which I will give here briefly:

The sitting patient puts the head down on a table, the ear to be examined upwards, and the face tilted slightly upwards again, to put the ampulla of the ipsilateral horizontal canal in the highest place. 1 cc. of ice water (0° C.) is instilled and the eyes carefully watched for the first flicker of nystagmus. Now the ear is emptied at once, nystagmus tested for the vertical and horizontal canals, past pointing and Romberg is noted, whereafter the moment of expiration of the induced nystagmus is observed. Now according to Atkinson the chief measure for irritability is the quotient between the duration of the caloric nystagmus and the latency, that is the time elapsed between the instillation of water and the first flicker of nystagmus. Normal is 3—4, higher is hyper-, lower is hypo-irritable. Vertigo and other subjective concomitant reactions are observed as well.

Atkinson claims simplicity, with which I can agree, having used this method before the war with satisfactory results. He claims exactness which favours comparison with data obtained by others. To obtain this he uses a special syringe being able to deliver 1 cc. only at a time, the syringe being cooled in advance so as to ascertain the right temperature.

I used a 2 or 5 cc. Record syringe with coarse blunted needle which was inserted halfway into the external canal to be assured that the water really reached the drum, of course after seeing to it that the canal was entirely free of obstructing material. The small syringe beforehand was submerged in a bowl with pieces of ice, starting without water. Moreover it was filled and emptied several times with the residual water obtained from melting, so that a temperature of 0° C. was approached as closely as possible when ultimately it was filled with exactly 1 cc. and immediately emptied in the external canal of the patient. A second person is necessary to do the timing, otherwise the examiner is hindered in his observations. Fortunately in Bandoeng we still possessed some refrigerators, so that ice always was available. In Batavia and Pakan Baroe it was not, neither was there a thermometer so that an occasional caloric test was very inaccurate and had chiefly qualitative value.

When a spontaneous nystagmus was present, difficulties arose in determining the latency and duration of the induced one. On starting the test, this was relatively simple. In the initial head position in Atkinson's method of testing the eyes were put in the extreme lateral position not eleciting the nystagmus, in which I found fixation of an object or figure or mark at least some meters away on the floor or at the wall, very helpful. For judging the moment of expiration it was necessary for the observer to remember a visual picture of the lateral eye position in which the spontaneous nystagmus just failed to be present. I found this method more exact and convenient than judging the moment of increase of a spontaneous nystagmus, not to mention the difficulties in determination of the exact moment of cessation of this increase.

On appearance of the first flicker of nystagmus the ear was emptied and thereafter the eyes observed with head inclined backward 60°, then immediately the head was brought 45° to the contralateral side in addition, to determine the presence of a rotatory component. If the induced nystagmus had every appearance to last a long time, it was observed in head position 30° inclined forward as well. Now the patient was made to rise and the Romberg test taken, after this in sitting position he was made to point in the vertical plane only, whereafter the moment of expiration was noted in head position 60° backward. When getting experience in this method there is ample time to do all these tests in the average patient. In the course of time before the Romberg test, the deviation test was carried out, in the sitting position with arms horizontally stretched in the sagittal planes, and any deviation of body and arms noticed.

In my experience Atkinson's test approximately equals the Kobrak method with 5 cc. water of 15° C. in stimulating power, with regard to nystagmus as much as to concomitant objective and subjective symptoms. In a control-series of 20 normal inhabitants of the camp quotients ranging from 2 to 6 were found. Thus, to remain on the safe side in diagnosing hyper- or hypoirritability, Atkinson's limits of 3—4 were enlarged to 2 and 6.

In his original article Atkinson does not mention in which head position the expiration of the induced nystagmus is awaited [2]. I calculated it in head position 60° backwards, in which the nystagmus is more marked than in upright position; the former position may easily produce a longer time than the latter on theoretical grounds; I did not try it out.

I used this method, and not Kobrak's, in peace time, because of greater simplicity and exactness; in captivity in addition because there was no thermometer available to obtain the exact temperature of the water to be used.

Turning tests were done in Bandoeng in some patients on a surgeon's stool, an otological turning chair not being available. This was stopped very soon for reasons to be explained later. Galvanic tests were completely out of question, as were

optokinetic, although Kuilman[65, 66] later succeeded in having an apparatus for optokinetic tests constructed in Batavia.

This description has been purposely detailed. Under prevailing conditions many tests were impossible and it is well to realize clearly what was done and what was not.

SUMMARY

1. Otoscopy, anterior and posterior rhinoscopy, mirror laryngoscopy and inspection of mouth and pharynx.
2. Search for spontaneous nystagmus, judging lateral gaze, degree of convergence, pupils and their reflexes.
3. Search for positional nystagmus (some of the patients).
4. Hearing: whisper distance; Rinne, Weber and Schwabach with tuning fork a 1.
5. Inflation of the tympanic cavity, where practicable.
6. Romberg, walking and pointing tests.
7. Atkinson's cold water test, including Romberg, pointing tests and deviation.
8. Turning test: a few patients only.
9. Ophthalmic examination (Schwartz).
10. General examination (Smitskamp, Jenner).
11. Neurological examination (Buitelaar†, Van der Hoeven†).
12. The „Meinicke Trübungs Reaktion" (M.T.R.) was done in many of these patients in the beginning, and in all cases of anisocoria and form anomalies of the pupils (Ten Seldam).

C. OBJECTIVE SYMPTOMS

1. Otoscopy, rhinoscopy, etc.

Only anomalies connected with vitamin and dietary deficiencies, and allied conditions will be described.

a. Otoscopy

In the majority of this group of 160 patients there were no abnormalities of importance in the drumheads.

Traumatic rupture

During the whole captivity I saw approximately 40 ruptures of the drum from blows by Japanese guards. It is true this was no deficiency, but certainly it was always connected with the proximity of Japanese, and as such worth mentioning. All but one closed, in which a secondary suppuration after 2 months gave rise to a subperiosteal abscess. Mastoidectomy was performed in this case with one carpenter's hammer and chisel, one curette and some general surgeon's instruments. Restitutio ad integrum of the drumhead and hearing was achieved, whereafter the patient was duly turned out on working parties at the railroad; he survived captivity. This was done in Pakan Baroe.

Effusions in the tympanic cavity

In the later stages of the war many cases of effusion in the tympanic cavity were observed, nearly all of them in the Pakan Baroe period. Thence I can give no statistics, but it occurred to such extent, that I was able to show a physician, asking me for such cases, 6 fresh ones in 2 weeks. The drums mostly were in normal position or slightly retracted; transparent, so that a beautiful line, or, after inflation, airbubbles were to be seen. The landmarks were always clear, the membranes mostly brighter than usual. There might be coryza, mostly there was not. Most of the cases had oedema to a greater or less extent. Therefore a liability to form effusions was taken into consideration, caused by hypoproteinaemia or lack of thiamin. The effusions were rather obstinate to inflation, also when performed with the face downward. The fluid by its mobility gave the impression of rather low viscosity, and was always clear.

Undue patency of the Eustachian tubes

Further in Pakan Baroe several cases of abnormal patency of the Eustachian tubes were observed in patients with severe loss of weight, which is explained by wasting of the submucous fat in the lateral tubal wall. This fatty layer was first described by Rüdinger in 1870. Undue patency is described in tuberculosis and senility with loss of weight (Scheibe[104]). Our patients complained of autophonia and a queer cold feeling inside of the drums when breathing through the nose. I suffered from it for a few months after contracting benign (!) tertian malaria and bacillary dysentery and having two attacks of each in one month. When breathing through the nose air currents were felt to reach the tympanic cavity. In some patients the drumheads could be seen to move slightly outwards on expiration and inwards on inspiration. When breathing through the mouth the fluctuations in pressure in the respiratory system were too small to elicit the subjective and objective phenomena.

b. Anterior rhinoscopy

A considerable number of cases with *affections of the mucocutaneous junction in the vestibulum nasi* were observed, as well in the group of 160 patients as apart therefrom. Many crusts, often honey-coloured, were formed. The epithelium was red, small denuded areas were present. This affection did not respond to treatment with ointment, but immediately so if "coramine" (diaethyl nicotinamide, vitamin-action identical with nicotinic acid) was given (Van der Meer). Rhinoscopy further yielded little or no particulars.

c. Mouth

The oral structures afforded a great many characteristic symptoms, in and outside the 160 group.

Perlèche,

or *angular stomatitis,* was often observed (28 cases out of 160). It started with thickening of the epithelium in the mucocutaneous junction at the angles of the mouth, these spots looked whitish. Then the thickened epithelium became sodden, small fissures appeared, mostly horizontal. They might reach a size of one cm. and more, reaching considerably further into the skin than into the red of the lips and the mucosa. Mostly, however, they did not exceed ½ cm. Crusts, sometimes honey-coloured, were formed on these lesions.

Cheilosis,

an affection of the vermilion of the lips, chiefly where the dry part is passing into the moist one (11 of 160). This zone is red, areas may be denuded of epithelium, small radiar fissures may appear. Crust forming may occur, although not nearly so frequent as in the angular stomatitis. The lips are often swollen.

Stomatitis,

having peculiar sites of predilection, namely: adjacent to the orifice of the mouth and in two strips facing the line of closure between the dental rows. The mucosa is angry red in these

places, over the whole area or, more often, in patches. Small submucous haemorrhages are not rare, ranging in size from a pinpoint to a grain of corn, scattered in groups; sometimes denuded areas are to be seen. *Aphthae* were rarely observed, *ulcers* once (case described below).

The gums and bony palate are mostly free, if there is not a concomitant cause for gingivitis, like paradentosis, dental tartar or caries.

Glossitis,

often starting at margins and tip, in later stages covering the whole dorsum in front of the circumvallate papillae. The tongue looks fiery red, often it is grooved and fissured, in other cases "bald" and smooth. It is often swollen, impressions of the teeth being marked. Aphthae are still less frequent here than in the other parts of the oral mucous membrane. Stomatitis and (or) glossitis occurred in 20 cases out of 160.

In Pakan Baroe a score of cases were seen with a *dark brown pigmentation* of the dorsum linguae, without preliminary use of any medicine or suspect food. The filiform papillae were not elongated. The discolouration passed away in some days or weeks. It was not conspicuously accompanied by other mouth lesions. I have never found this phenomenon described in the literature and do not know its significance, neither whether there is any relation with the canine black tongue caused by nicotinic acid deficiency. Justin-Besançon describes a "blackish" tongue and lips in pellagra [53].

Salivary glands and ducts

There were in Pakan Baroe several cases of *acute swelling of the parotid* and occasionally also of the *submaxillary glands*, with or without an (evident) attack of malaria. It caused little pain, and was little tender on palpation. The secretion and colour of the saliva was normal, a small blunted probe entered normally into the ducts. These periods of swelling lasted for some days. Some patients had several of such periods. The swelling was not increased by mastication. The lacrimal glands were normal. Sometimes *swelling of the testis* accompanied it and mostly caused more pain; tumefaction of this structure alone was also observed several times. Manson Bahr describes orchitis with malarial parasites found in post mortem examinations [74]. Practically everybody in Pakan Baroe was a well-seasoned sufferer from malaria. Castellani and Chalmers describe an orchitis complicating subtertian malaria (malaria tropica), the testicles being only slightly swollen but very tender; and the patient is very ill [20]. This was not so in our cases.

There seemed to be a relation between the swelling of the salivary glands and that of the testis, in that sometimes they occured simultaneously. In other cases a patient having had an orchitis, some weeks later developed swelling of some or more salivary glands. There was no preliminary or concomitant dryness of the mouth. It was not mumps since it would relapse in one patient. Suppuration was never observed except in one case where both parotid glands excreted large quantities of thick and yellow pus, without a concretion or any other obstruction of the ducts being apparent. This suppuration lasted for months, (case observed by Bruining in Tjimahi and Batavia); thereafter I lost contact with the patient.

Further I saw 4 cases of acute *obstruction of the Whartonian duct.* In 3 of them a grating sound was elicited by a blunt probe and a stone removed, twice by slitting the duct on the probe; one, which was very near the submaxillary gland, by incision of the floor of the mouth on the probe. This case healed with a fistula from the duct to the floor of the mouth, immediately above the previous bed of the stone, a piece of duct in front thereof lying idle. In the fourth case the probe entered about 1½ cm. and stopped abruptly there, grating was not elicited. On slitting the duct a caseous particle of pinpoint size was found, on removal of which an abundant flow of clear saliva poured out. The complaints vanished instantaneously and lastingly.

This is a rather large number of obstructions to observe in two years (the last two of captivity); I saw only one small concretion in 8 years of busy practice in the tropics under normal conditions. I could find nothing on the influence of malnutrition on sialolithiasis in the literature; certainly there were too few cases to assume a connection. The swelling of salivary glands described above is not mentioned in malaria; Andrews describes occasional swelling of the parotid glands in pellagra [1a].

d. Pharynx

The distribution of the lesions is characteristic again. The mucosa is *angry red*, more or less swollen, most marked on the uvula and its surroundings. From here the redness fades away forward onto the soft palate and laterally and downwards onto the faucial pillars. The tonsils are not or little too red. *Aphthae* may, rarely, be encountered. This affection is less common than the preceding ones (3 of 160).

e. Larynx

Laryngitis

This affection is still less frequent. *Redness* and a little swelling of the epiglottis, notably its margins, and of the ary-epiglottic folds are the objective findings.

Paralysis

Towards the end of captivity several cases with *hoarseness* were seen, in which there was *paresis* of one or both posterior

crico-arytenoid muscles. The cords moved sluggishly and only to a small extent outward. There was no dyspnoea distinctly due to lack of abduction of the vocal cords. It was mostly present on effort, though, but gave the impression of being dependent more upon extreme weakness (paresis) of several groups of muscles and (or) insufficientia cordis. The underlying pathology of the hoarseness lay in the vocal cords, which failed to close properly, an ovally shaped space remaining between them; the edges were not sharp, the cords looked flabby (weakness of internal thyro-arytenoid muscles). There were also some cases with paresis of abduction without hoarseness and two with *paralysis* of abduction on the left side. One case with both cords in cadaveric position was observed. In the other cases the left recurrent nerve was often damaged to a greater extent than the right one.

Comment

Although there were not many patients of this kind, about 10—15, there seemed to be a distinct preponderance of the intensity of the lesions in the left, over those in the right recurrent nerve. In some of these perhaps cardiac dilatation could be made responsible for this difference, in others, however, there was no anatomical cause to be found, while the avitaminosis must be influencing both nerves equally. In the latter cases the following explanation is attractive.

It is known that of two nerves injured to the same degree, the longer one undergoes the greater change; the ability of a nerve to resist injury is inversely proportional to its length. Since a few regenerating fibres are constantly found in the peripheral nervous system of normal individuals it seems reasonable to assume that new fibres are continually replacing those which have worn out. A new fibre is growing as rapidly as 1—2 mm. a day (Bing[13]). Consequently long nerves will consist of older fibres than short ones. The nearer a fibre is to its time of death, the more vulnerable it most probably will be to injuries. In this way an explanation of the greater vulnerability of longer nerves is given.

Another explanation why the longer nerve is more vulnerable, is the following: a longer nerve, especially the left recurrent, which dips deeply into the thoracic cavity, with many neighbouring structures to pass, may suffer from pressure more readily than a short one. This may be so little marked, that in ordinary circumstances there is no evidence from this fact. However, as soon as the entire nervous system is harmed by avitaminosis, such pressure may be the drop which causes the overflowing of the bucket. These cases of slight injury, normally borne without harm, but in the camp causing serious loss of function, were observed several times in peripheral nerves of legs and arms.

In *beriberi* aphonia is repeatedly mentioned, especially in infants, where it mostly is attributed to laryngeal oedema. In chronic adult cases hoarseness is common as well, degeneration of the Xth nerve and its laryngeal branches are frequently found (Bicknell and Prescott[11]). Clinically also the hoarse voice is here often found to depend upon neural lesions. Eddy and Dalldorf, apart from the mentioned facts, report laryngeal paralysis also in infants, the left cord being more frequently involved (Ohta)[33]. Laryngeal oedema was never observed in our cases (all adult chronic ones).

f. Oesophagus

There were many complaints of *burning and pain* behind the sternum on swallowing. We could not perform oesophagoscopy, but in several post mortem examinations there were big red patches in several places of the oesophagus, consisting partly of haemorrhages, partly of dilated small vessels. Fisher[37] found oesophageal lesions in living pellagrins, Justin-Besançon[53] also. Interesting is the tendency to bring Plummer-Vinson's syndrome into the pellagrous symptomatology (a. o. Manson Bahr[74]).

g. General remarks, pathology

All these symptoms tended to come and go in waves, lasting some weeks or months, vanishing by untraceable causes and appearing again for some reason or even without one. Notorious

to precipitate an exacerbation were periods of extra bad food, an attack of malaria or dysentery; and drafts, journeys arranged by the Japanese being periods of more intensified malnutrition, filthiness, exhaustion, lack of sleep, thirst, and fear for torpedoes.

All sorts of combinations of the described affections occurred. They went frequently with periods of diarrhea, thus giving proof of the fact that no part of the digestive tract, from lips to anus, is exempt from this disease. In several post mortems (L. Simons) confirmation of this could be obtained. The findings were: extreme atrophy of several parts of the gastro-intestinal tract, each covering one to two meters, slowly shading off into normal parts. This atrophy, so marked, that the intestinal wall could be as thin as sausage-skin, might be found in otherwise well nourished bodies (see Eddy and Dalldorf [33]); although in other cases there was frequently extreme emaciation. Submucous haemorrhages and dilated vessels were common. A dark grey pigmentation was often found in several places in the large and small bowel, most marked in the caecum. It consisted of small round stipples, nearly of pin point size. Ulcers were never observed but in the large intestine of many cases, a dysenteric aetiology being quite possible. The other abnormalities, as said before, occurred in the whole digestive tract, from lips to anus; in one patient more marked in certain parts, in another in others.

One patient with the typical lifeless, staring, pellagrous gaze was observed who developed two outbreaks of ulcerous stomatitis with the characteristic distribution in the course of one year. Each disappeared without traceable cause. They were not accompanied by diarrhea. Food intake was seriously interfered with by pain. Nevertheless he managed to come out of this apparently solidly closed vicious circle. The third exacerbation left his mouth alone but affected his bowels and precipitated his death. No ulcers were found in the gastro-intestinal tract, but many other abnormalities, such as described above.

Eddy and Dalldorf [33] describe the abovementioned dark grey pigmentation in pellagra. Herzenberg regards it as typical for the disease [50]. They are found in only one other disease, sprue, and there infrequently [33]. Microscopically, they prove to be cysts formed of distended Lieberkühn's crypts. (See also Ceelen [21] and Denton [29]).

Atrophic conditions are to be observed also in mouth and

lips after some exacerbations have taken place. The mucous membrane becomes thin and whitish in irregular patches. None of the theories on pellagra can explain the sudden spontaneous remissions and the invariable reappearance of all these symptoms, which Eddy and Dalldorf also describe in pellagra and especially in black tongue [33]. In our cases there was no distinct relation to seasons. In the tropics there are only two of them, one wet, one dry.

Conspicuous is the tendency of the disease to touch the surroundings of orifices and of passages from one structure into another. We see this in the nostrils, in the mouth, at the pharyngeal pillars, the laryngeal orifice. Post mortem we find the same tendency; more severely affected are the surroundings of the cardia, pylorus, caecum and anus. The same again is seen in balanitis, urethritis and vulvitis, described in this deficiency [11, 33, 128]. A traumatic cause supervening on the avitaminosis must be taken into consideration. In our post mortem examinations (L. Simons) it was conspicuous that there were haemorrhages and redness on the oral side of Kerkring's folds of the intestine, as if the trauma of the moving masses of food had brought them out.

Thrush

Thrush was often developed on the severely inflamed mucosa of mouth, tongue and pharynx. The type of lesion was not always the same; it might vary from nearly white to yellowish brown. Mycelial threads and conidial forms were always found in abundance. Sometimes there were patches, varying in size from a pin point to a grain of corn; again there were threads, forming an intricate web. It disappeared within 2 × 24 hours, mostly in one day, by one or two applications of gentian violet 1 %. Then there was considerable alleviation of pain also. We failed to find this affection in the oesophagus post mortem, but we performed no such examination in cases suitable in this respect. From alleviation of retrosternal pain by making the patients swallow their saliva after application of gentian violet on the oral lesions, we gained a strong impression that the mycosis was present in the oesophagus as well. A few cases of thrush were observed in less debilitated people, but mostly it was a certain precursor of death.

Castellani found that thrush may be caused by the following mycoses:

Fungi imperfecti: Genus monilia Persoon
oidium Link
hemispora Vuillemin

Ascomycetaceae: Genus endomyces Link.

Generally the affection has a whitish colour; some varieties of oidium and monilia, however, may be yellowish.

The mycoses grow deeply into the mucosa, which explains the adhesion and the pain [20].

COMMENT, ARIBOFLAVINOSIS

Perlèche, cheilosis and certain affections of the oral structures are attributed to riboflavin deficiency by many authors. The latter group of affections differ from those in pellagra by a magenta, livid colouration of the mucosa. Personally I never saw this distinctly, although there were cases in which the red colouration was less angry and more dark. Perhaps they are those described as "magenta". Unfortunately in these cases, which were observed in Pakan Baroe, we had no opportunity to try out differences between nicotinic acid and riboflavin treatment. In Bandoeng, however, Van der Meer was in the position to treat a considerable number of cases, of which I saw the greater part, with "coramine", the diaethyl amide of nicotinic acid, in doses from 1—2 cc. daily intravenously. Within one to two weeks the majority was completely relieved, from their stomatitis as from the perlèche and cheilosis, which latter lesions are considered as pathognomonic for riboflavin deficiency (Bicknell and Prescott[11], Manson Bahr[74], Stepp und Kühnau[128], Eddy and Dalldorf[33], Stannus[125] and many others).

Food lacking nicotinic acid, often lacks riboflavin, thiamin and pyridoxin as well. It is clear without further comment that in nature mostly complex deficiencies of the B group occur. Apart from this the impression is obtained that several vitamins from the B group to a greater or less extent may, by their absence, elicit the same or similar lesions.

Van der Meer's observations in Bandoeng point strongly in this direction, in that perlèche and cheilosis disappeared on diaethyl nicotinamide, whereas many others saw them vanish on administration of riboflavin, and Eddy and Dalldorf mention their disappearance on pyridoxin also (Smith and Martin[33]). Machella and Mac Donald failed to improve 13 cases of perlèche with riboflavin. Some responded to nicotinic acid, B_6 and yeast[11]. On closer examination this is not as strange as it looks at first sight, thiamin, nicotinic acid, riboflavin, and pyridoxin each working very similarly in the intracellular dehydrogenation of carbohydrates[11, 33].

There were many patients with photophobia, lacrimation and burning and itching of the conjunctivae. Circumcorneal and later peripheral corneal vascularisation is generally considered as a specific sign of ariboflavinosis[140, 33, 74], although Bicknell and Prescott[11] on account of more recent investigations on the subject do no longer agree, both phenomena being observed in many normal people as well, and not disappearing on administration of riboflavin. Whatever it may be, this affection is only to be demonstrated by the slit-lamp, which was not available in the camps we were. It might be a cause for the frequently occurring lacrimation, photophobia, itching and burning, but mydriasis also might play a role (see below).

SUMMARY

Eczema vestibuli nasi, angular stomatitis, cheilosis, stomatitis, glossitis, pharyngitis and inflammation of the entrance of the larynx were frequently observed. Analogous affections were demonstrated in the oesophagus, stomach and intestine in post mortem examinations. The affections formed many varied mutual combinations. Scrotal dermatitis was a frequent concomitant symptom.

In the group of 160 patients 53 showed or reported affections of nose, mouth, pharynx or scrotum, or combinations of them.

2. Nystagmus

a. General remarks, definitions

By *nystagmus* is meant a to and fro movement of the eyeballs, in which in a certain direction of gaze an equal amplitude and frequency is sufficiently maintained to achieve regularity.

This regularity is not an obligatory point in the literature (see for instance Klestadt[55]), but it will be here, because irregular forms of nystagmus were brought out under another name in this investigation. Confusion is feared to be the result from trying afterwards to take out the forms of irregular nystagmus which certainly form part of the picture of nystagmus. In the main Klestadt's „Nystagmuszer-

gliederung" is meant here, to which we will return later.

When there is a quick and an opposite slow phase, the nystagmus is called *rhythmic*; when both phases are equally fast, *oscillatory* („Pendelnystagmus" of the Germans). When speaking of nystagmus only, the rhythmic one is meant.

Unfortunately the *direction* of the nystagmus is denominated by the direction of the quick phase, because this is the most conspicuous one. Högyes in his classic experimental studies of 1881 denominated the nystagmus by the direction of its slow phase (Klestadt[55]), which is the essential and in most cases the primary one, certainly always so in vestibular nystagmus. Of course we will adhere to the regrettably adopted custom of denomination by the direction of the quick phase.

According to the plane(s) in which the nystagmus beats, it is called *horizontal, rotatory, horizontal-rotatory, vertical* or *diagonal. Retraction nystagmus* is a movement of the eyeballs in the horizontal plane, quick phase backward and slow phase forward, a rare form (Brunner[16]).

The *frequency* may be recorded in the number of beats per minute; or, more commonly, as quick, moderate or slow.

The *amplitude* may be expressed in millimeters, or, more usually, differentiated in coarse, medium or fine. Mostly the amplitude is inversely proportional to the frequency.

The *intensity* is determined by amplitude and frequency.

By *vestibular nystagmus* is meant a nystagmus elicited anywhere in the chain: labyrinth, vestibular nerve, vestibular nuclei, vestibulo-mesencephalic tract (in the posterior or medial longitudinal bundle), connecting the vestibular nuclei with those of the extraocular eye muscles. Perhaps middle ear and tubal affections should be added, but they may elicit nystagmus only by direct action on the labyrinth. By *peripheral vestibular nystagmus* is meant a nystagmus elicited in the labyrinth or in the vestibular nerve, by *central vestibular nystagmus* such as is provoked in another link of the above-mentioned chain.

The vestibular nystagmus always shows a rhythmic character, and is rendered more marked by looking in the direction of the quick phase; the reverse, however, is not true of both statements.

Any nystagmus showing itself only when looking in the direction of the quick phase, is said to be of the *first degree*, when present also in gaze straight ahead *second degree*, when present in all directions of gaze *third degree*.

Nystagmus is called *spontaneous* when it is present without artificial irritation (it may be present only on looking in a certain direction); *induced* or *reactive* when it appears after stimulation of some kind, such as turning, galvanic or caloric irritation of the labyrinth.

The same applies to past pointing, walking and Romberg test.

The French distinguish a spontaneous nystagmus *sensu strictorii*, appearing in gaze straight ahead, from a "nystagmus révélé", translated *revealed nystagmus*, when appearing only in an eye position other than central (Aubry[4]). Thus no first degree nystagmus can be spontaneous. We will use spontaneous in the sense of not induced, although the French definition appears to be quite rational.

After these introductory remarks we will consider the question of 1st degree nystagmus. Second and third degree nystagmus were seen in three cases only, and gave no difficulties like those arising in classing a 1st degree nystagmus as pathologic. The question of physiological nystagmus in extreme position of the eyes was borne in mind all the time, and this position avoided in examination on nystagmus, while it was used *after* this examination (to avoid fatigue in nystagmus tests) to judge the strength of lateral gaze. Yet it must be admitted, that in most cases nystagmus occurred only in an eye position not far from the extreme. Certainly there were many cases in which it showed itself in a position considerably remote from the extreme lateral one.

Klestadt[55] mentions nystagmus by fatigue (Ermüdungsnystagmus) and correction nystagmus as two forms of non-vestibular and physiological phenomena.

Nystagmus by fatigue of the lateral gaze is described by him as a slow revolution back of the eyeballs from the extreme lateral position, with quick return of the eyeballs to the lateral position again; this repeated regularly results in a rhythmic regular nystagmus. Sometimes group forming is seen in this form. Occasionally the excursions are very small. Then

the difference between slow and quick phase disappears and the nystagmus becomes fine oscillatory, in any case if observed with the naked eye. Klestadt writes further: Often this nystagmus is elecited only after keeping the eyes some time in the extreme lateral position, in other cases it cannot be provoked. Many people bear the extreme position with absolute quiet eyeballs for a remarkably long time, in others nystagmus is appearing in less than a minute, sometimes longer. On the incidence of this sort of nystagmus quite different figures are given: from 60—75 % (Schultz, Offergeld) over 50 % (Mygind) and 6 % (Streit[131]) to 0,3 % (Youngerman[144]) (taken from Klestadt[55] not verbally). Unfortunately most of the original articles of the authors giving statistics hereon are not available to me, so that I am not able to form an opinion on the cause of the discrepancy. The findings of Streit and Youngerman are in any case not comparable, starting from quite different material and the latter using Frenzel's spectacles in observation[144], the former not[131].

Bielschowsky states: "This *physiological nystagmus* is precipitated by extreme lateral gaze and depends hereon, that the maximal innervation can be accomplished only for a short time. In relaxing of this innervation the eyes go back somewhat towards the middle position, a new innervation impulse is driving the eyes to the point of fixation again, into extreme position. This *extreme position nystagmus* ("Endstellungsnystagmus") is in some way the analogy of that nystagmus, observed consistently in paresis of conjugate eye movements"[18].

Aubry demands observation behind Bartels' spectacles to eliminate a "nystagmus de fixation" (probably meaning the "Einstellungsnystagmus" of the Germans = correction nystagmus), and not surpassing an angle of 45°—50° from the middle position to eliminate the physiological nystagmus ("nystagmus physiologique") in extreme lateral position. In his opinion this physiological nystagmus is always absolutely symmetrical on both sides in the two lateral directions of gaze[4]. Klestadt, however, writes: "It is often present in both directions in which it is not always equally

marked to the right and to the left (Mygind, Ruttin); often it is beating to one side only. Changes in eliciting this nystagmus, in its plane of beating, and in its direction occur in the same person"[55]. With regard to the symmetry, Streit[131] is of the same opinion as Klestadt.

In the literature there seems to be agreement with respect to the fact that the only essential difference between this "physiological" nystagmus in extreme position and the nystagmus in paretic lateral gaze (among others described by Frenzel[38]) is that the former appears in extreme position only, and the latter already in a position less remote from the middle line, in marked cases even immediately past this line. It is evident that this difference is only a quantitative one. Frenzel classifies the critical lateral position for assumption of pathologic nystagmus as "zwangslos", perhaps best translated as "unstrained"; Aubry[4] as "not more than 45°—50° deviating from the middle line". "Unstrained" is a subjective sensation of the patient; a position having this quality for a normal individual, may be very annoying for one with weakness of lateral gaze, whereas speaking anatomically, both pairs of eyes are approximately in the same degree of abduction. Therefore in my opinion Aubry's classification is more exact, although in practice it is difficult to estimate 45°—50°; the real position possibly being, that he obtained a visual picture of this critical eye position in the orbits by long experience, but to communicate this position to others, saw no better method than estimating the angle of deviation.

What I want to arrive at, is this, that there must be a gradually passing from this physiological nystagmus in end position, over the slightest degrees of nystagmus in weakness of lateral gaze, to that in paretic gaze. In the former case a normal neuro-muscular apparatus cannot satisfy an abnormal demand; in the latter a too weak conjugate eye movement cannot fulfil a normal requirement. Between these two, smoothly graduated transitional steps may be expected. In addition, the physiological nystagmus cannot be elicited at random in any individual. If all this is true, this "physiological" nystagmus should be called physiological only in the absence

of other connected symptoms, a clearly cut boundary between the two forms being absent.

Of course in the marked cases of nystagmus in paretic gaze, which show coarse excursions, sometimes immediately when the eyes are brought out of the middle position (F r e n z e l [38]), there is no difficulty.

Correction nystagmus (Einstellungsnystagmus) consists of aiming movements to bring the image of an object lying in a peripheral zone directly on the fovea lutea. Under some circumstances these aiming movements become visible and may show a rhythmic character. It is seen in abduction of the eyes, the quick phase is the primary one, theoretically, which fact, however, cannot be recognized. The difference from nystagmus by fatigue is that the correction nystagmus ceases after some time, and shows itself immediately on abduction of the eyes, whereas the other mostly occurs only after some exertion of the eye muscles by remaining some time in the lateral position, or by moving the eyes in the opposite abduction and back again; further the latter has a tendency to increase instead of to decrease. For the rest these two forms may easily mix (K l e s t a d t [55]).

The *nystagmus in paretic gaze* (Blickparetischer Nystagmus, see for instance F r e n z e l [38]) may be elicited by lesions anywhere in the chain: cortical centre at the foot of the 2nd frontal gyrus, capsula interna, cerebral peduncle, posterior longitudinal bundle, nuclei of the extraocular eye muscles. Mostly it has coarse excursions, although in minor grades they may be fine. In middle position the eyes are quiet, also behind F r e n z e l's spectacles, which is an essential point of difference with (first degree) vestibular nystagmus, consistently showing itself under these conditions as well. This includes another point of difference from vestibular nystagmus. The paretic nystagmus being mostly coarse in lateral, and always absent in middle position, declines rapidly from considerable excursions to zero in moving the gaze from abduction to straight ahead. Vestibular nystagmus of coarse amplitude in lateral position mostly is present also in middle position, thus decreasing much more slowly (no spectacles). This is the reason, why with coarse nystagmus in lateral and

quiet in middle position neurologists and ophthalmologists immediately think of paresis of gaze. A vestibular nystagmus of small amplitude in the lateral position shows itself mostly also in the middle position when observed behind F r e n z e l's spectacles. More strongly still: F r e n z e l states that in cases where no nystagmus is present on ordinary observation in deviated eye positions, a vestibular nystagmus may be uncovered in the middle position behind his spectacles [38].

There is a form of nystagmus which is revealed in more than one direction on examination in the four directions of gaze, always beating in the direction of the gaze. This is called "Blickrichtungsnystagmus" by F r e n z e l; *"nystagmus multiple"* by the French (Aubry [4]), when it is beating in at least three directions; in other words there is always a vertical component, be it upwards, downwards or both. When existing in the two lateral eye positions only, it is called *bilateral nystagmus*. It may or may not be more marked in one direction; may be either central vestibular, or paretic, or mixed. In this multiple nystagmus then, when paretic, the eyeballs are always quiet in the middle position, also behind F r e n z e l's spectacles; in cases of vestibular origin a more marked component is showing itself under these conditions. The French call this more marked and persistent component *"nystagmus prédominant"* (Aubry) which is clear without further explanation.

In other words, a vestibular nystagmus, (also when being the more marked component of a multiple nystagmus), while being of the first degree without spectacles, becomes of the second degree when fixation is excluded. Paretic nystagmus can never be of the 2nd or 3rd degree.

Fixation may suppress a vestibular nystagmus. On the other hand it may elicit nystagmus of rhythmic character, as is the common opinion for correction nystagmus. It seems strange, that this occurs in lateral position of the eyes only, and never in middle position. This fact suggests influences eliciting the slow phase, analogous to those in paretic and fatigue nystagmus. Whatever the true mechanisms in all these forms of rhythmic eye movements may be, it is always wise to include F r e n z e l's spectacles in observation of nystagmus, although F r e n z e l himself thinks to see advantage

in not using them in judging paretic nystagmus in eye positions other than the middle one. These spectacles would have been a priceless differential-diagnostic instrument in our investigation; while now we shall partly have to be satisfied with guesswork.

Positional nystagmus is a nystagmus evoked by a certain position of the head (type I Nylen[88]); or it may be an increase of a spontaneous nystagmus by the same cause (type II Nylen). De Kleyn[56, 58, 61] distinguishes five forms, among which:

vestibular positional nystagmus, elicited by certain head positions in respect to gravitation, movements of the head in regard to the body being excluded;

positional nystagmus by neck reflexes, evoked by a certain head position in regard to that of the body, the influence of the force of gravitation not being changed;

positional nystagmus by vascular disturbances at the base of the skull, brought about by turning the head in a certain manner in respect to the body[58].

A complete examination on positional nystagmus is rather intricate and very time consuming. According to Klestadt positional nystagmus is as often of central origin as peripheral[55], Seiffert[55] and Burger[17] consider it to be always central, Aubry[4] and Leidler[69] as mostly central.

b. Observations in our patients

Under this heading only the forms with regularity will be described.

The nystagmus was nearly always *rhythmic*, only 2 cases were seen with *horizontal fine-oscillatory* nystagmus on looking upwards and 2 with the same sort of nystagmus on looking laterally. One of these latter patients developed a rhythmic nystagmus later.

The plane of beating was *horizontal* in most cases; also *horizontal-rotatory* nystagmus with a slight rotatory component was observed, less frequently still one with a marked rotatory component, and never pure rotatory.

The nystagmus was most often *bilateral*, beating to the left on looking to the left and to the right in that lateral eye-

position. In these cases it was mostly asymmetrical; being more marked in one direction than in another. However, there were also many cases with nystagmus in one direction. Diagonal, vertical and retraction nystagmus were never observed.

The *amplitude* was mostly fine to medium, although there were a considerable number of cases with marked amplitude, ± 3 mm., and 2 cases with an amplitude of nearly one cm., in an acute attack (record no. 38).

On one of these 2 cases no record is available, the case will be briefly described here. It concerned a „healthy" man of 40 years, participating consistently in physical training. One day, while performing to and fro rotating movements of the body with legs spread apart and body bent 90° forward, he suddenly sat down and, laughing, stated: "Well, I'm a little dizzy". The whole group was sweating and so was he. There was no tinnitus, deafness, sickness, vomiting, or compulsary position. Neither was his general well being severely disturbed, on the contrary, a few minutes later he went on with the exercises. Besides the apparently slight vertigo and the sitting down, he showed a horizontal nystagmus which laymen saw from 10 yards distance. I was in the same group: the nystagmus was horizontal with oscillations about one cm. long, of high frequency and of the 3rd degree. The eyes were dragged back by the slow phase until considerably past the middle line. The attack passed away in a few minutes, the nystagmus rapidly subsiding to 2nd and 1st degree and disappearing.

What was found on examination, conducted a few hours later, I unfortunately cannot remember completely. No caloric and turning tests were performed. Middle ears and hearing were normal. This man the next and the following days did the identical exercises again and again without further mishap.

Not infrequently distinctly longer oscillations were observed on that eye to the side of which the patient was looking. The length of the excursions on the homolateral eye (it may be called thus for the sake of briefness) might be 2 and even 3 times as long as that on the other eye. On reversing the direction of gaze the longer excursions moved to the other eye, i. e., the homolateral one again. I could find very little in the literature either on this phenomenon or on its significance. Wechsler[142] mentions the possibility without further comment, Bing[13] states briefly that some authors explain this to be cerebellar lesion on the side of the bigger excursions, although Bing himself never obtained any confirmation of this.

The *degree* was nearly always first; the 2 cases with extremely coarse oscillations were 3rd degree; one patient with 2nd degree nystagmus was seen, a case of Wernicke's encephalopathy

(polioencephalitis haemorrhagica superior), described under neurological examination. There were several cases, however, in which the nystagmus appeared in a lateral position not far from the middle line (20 of 160), although again it must be stressed that mostly it appeared only in an eye position not far, but distinctly, short of the extreme lateral one.

The *direction* of the nystagmus then, was nearly always the same as the direction of gaze. Exceptions confirming the rule were the 3 cases of nystagmus of higher degree and the 2 with horizontal-oscillatory nystagmus on looking upwards.

The *frequency* in general was medium with inclination to quick, mostly inversely proportional to the amplitude. The 2 cases of 3rd degree nystagmus with long amplitude, however, had a considerable high frequency also, thus the intensity of the nystagmus was very marked. Very slow movements were never seen in this type of nystagmus with regularity.

The *intensity* was mostly slight to moderate, in accord with the statement on frequency and amplitude. However, it might be extremely high in attacks. In these cases either there might be severe accompanying subjective vestibular sensations, or these might be very little marked (case described above). In cases with moderate intensity, they might be nearly or completely missing.

An *eyelid nystagmus* on all four eyelids was not infrequently observed to accompany the nystagmus of the eyeballs. It was always most marked in the medial part of the lower lid and consisted of small contractions synchronous with the quick nystagmus phase and directed towards the median plane. Van der Hoeven† observed one case of *head nystagmus*, which he and I unfortunately did not observe again in a reexamination performed later. Neither could the phenomenon be evoked by caloric stimulation. Palatinal nystagmus was never observed.

In most cases there was no influence from head position on the nystagmus. One case was seen in which a third degree horizontal nystagmus could be provoked by bringing the head or body and head right side down after a latent period of a few seconds (case no. 38, *type I Nylèn*). Because of severe concomitant subjective sensations it could not be determined

whether this *positional nystagmus* would remain as long as this head position was maintained. The patient immediately did all he could to alter the position. We had the greatest difficulty to persuade him to have this phenomenon elicited once a day. In two other cases there was a definite increase of a spontaneous nystagmus in both lateral positions of the head (or body and head). When lying right side down the spontaneous, first degree nystagmus to the left became more marked, though not yet second degree; and inversely (*type II Nylèn*, record no. 18). In all of these three cases there was increase of vertigo in the critical position. In one of them this increase mounted from zero to a severe dizzy spell.

A characteristic point in many of the patients was the *variability* of the nystagmus, with regard to existence, intensity and direction. One day bilateral nystagmus had a more marked component to the left, another day to the right. Or a unilateral nystagmus changed its direction from one side to the other and back again. Or a nystagmus being present one week, was gone the other week, coming back again later. Once a patient was seen with a nystagmus of marked amplitude disappearing and emerging again several times during examination over ½ hourly periods (no. 22). Transition from a horizontal nystagmus in a horizontal-rotatory one, or inversely, was never seen.

There were a number of patients, who on the first time looking laterally, showed no nystagmus, but did so definitely after having repeated the lateral gaze 2—4 times. All the time the extreme eye position was avoided. The nystagmus elicited this way by slight exertion of the eye muscles, might be quite marked, although never of the second degree. This form is approaching the fatigue nystagmus very closely, the difference being only this, that the extreme position was avoided. This symptom was called *praenystagmus*. With general improvement of the patients' condition a nystagmus was often disappearing through a phase of praenystagmus, the reverse being true as well.

At the first examination 70 patients showed a nystagmus of one of the patterns described above, 34 a praenystagmus. As will be evident from the preceding, these figures varied in

the course of time. Over the whole period of observation, these figures were 94 and 48 respectively. Of the patients with praenystagmus nearly all showed either correction nystagmus, nystagmoid, weakness of lateral gaze, or combinations of them on looking laterally for the first time.

The strength of lateral eye movement was so weak, that not infrequently the following occurred: In testing for nystagmus in gaze straight ahead, it was negative. On leading the eyes to the left: correction nystagmus; on moving them to the other side; nystagmus. It often gave the impression that the balance was disturbed by the first movement to the left. This means that the nystagmus on looking to the right possibly would have been a correction nystagmus or completely absent, if we had commenced with the eye movement to the right. On leading the eyes to the left again there might appear a lasting nystagmus, sometimes quite marked. In other cases, certainly, nystagmus was only revealed by repeating the above-mentioned procedure once or twice.

For these reasons a correction nystagmus was considered as suspicious, notably when appearing only in one lateral eye position; but, of course not as pathological. All these results were obtained in medium lateral positions, not extreme. I may be forgiven for stating this again and again, but it is the only and cardinal point of difference between "physiological" and pathologic nystagmus.

It will not be amiss here to stress that no patients were seen with typical rotatory vertigo without nystagmus during the attack; but that 31 patients with distinct nystagmus, first degree, horizontal or horizontal-rotatory, failed to experience any trace of dizziness. Further, in many other cases nystagmus of moderate intensity was accompanied by only slight sensations of dizziness, and variations in intensity of the nystagmus were not accompanied by proportional changes in vertigo.

3. Nystagmoid

By *nystagmoid* is meant here a to and fro movement of the eyeballs with an intricate type of regularity or without any regularity at all, only a slow phase from the lateral eye position towards the middle one always being recognizable. Frequency, amplitude and velocity of the nystagmoid eye movements were variable. In looking for them the extreme lateral eye position was also constantly avoided. As a matter

of fact these movements of course were observed during testing for spontaneous first degree mystagmus.

In some the eyes revolved slowly back, like floating in slowly moving water, often to a point very near the mid position. Then with a jerk the lateral eye position was assumed again. There might follow 3—5 regular, rhythmic nystagmus beats with moderate frequency and amplitude, then the floating back intervened, and so on. This form bears striking resemblance to Klestadt's[55] *"Nystagmuszergliederung"*, also described by De Kleyn[59] as *group forming* in nystagmus. Unfortunately at the time of this investigation I did not know the existence of this phenomenon. All cases without regularity therefore were brought under one heading, nystagmoid.

In other cases the eyeballs were observed to float back in the same manner, a recovering jerk occurred, they revolved back again, covering a shorter or longer distance, and so on, so that there was no regularity. Or: after the first recovering jerk the eyes remained steady some moments in the lateral position, then floated back, many combinations being possible, in which the conformity was that there was difficulty in maintaining a lateral eyeposition which for a normal person would have given no trouble.

In other patients again there were periods of rhythmic nystagmus of small amplitude and high frequency, alternating with periods of longer excursions and lower frequency. The intensity then, remained more or less the same. Each period would cover 5—10 beats.

In another group again there was no system at all to be discovered in eye movements elicited by lateral gaze, but for the slow backgliding towards the middle position.

All the described forms objectively had in common the slow revolution back of the eyes from a lateral position easily maintained by a normal individual. When regular nystagmus beats appeared (for a short period) the distance covered by this slow movement was moderate to small; in the other cases it was considerable and might come to very close to the middle position.

These patients numbered 67 out of 160. In a number of

them definite regular nystagmus was elicited by slight exertion of the neuro-muscular apparatus governing lateral conjugate movements of the eyes: praenystagmus.

COMMENT

Klestadt describes group forming in spontaneous nystagmus ("Nystagmuszergliederung") in paresis of lateral gaze, although mostly it is seen in this condition in induced nystagmus only [58]. (See comment on caloric stimulation).

Turning and galvanic current are more liable to elicit group forming than caloric stimulation. He also observed this in cases of disseminated sclerosis [58]. De Kleyn [59] observed group forming in a girl with inconsistent spontaneous second grade nystagmus, occurring also in nystagmus induced by turning. Affection of the central nervous system was evident from concomitant phenomena and the history. The author states: "Most probably when attention is paid to this symptom, such group forming will be observed more frequently in affections of the central nervous system. Possibly then also the cause may be determined."

4. Weakness of lateral gaze

By *weakness of lateral gaze* is meant more or less severe difficulty, subjectively and objectively, to reach or maintain the extreme lateral eye position. In these tests a purposive attempt was made to make the eyes occupy the extreme positions.

In these patients unpleasant sensations were brought about by this direction of gaze, in several cases extremely so. An attack of dizziness or headache might easily be evoked. Many patients immediately started winking or closed both eyes convulsively at once; phenomena which made the observation difficult and sometimes impossible. Tears ran down the cheeks; profuse sweating, sickness and occasionally vomiting might follow. These men strongly disliked the examination. In rare cases they began to weep. These sensations might occur in a varying angle of deviation from the middle position.

Often *diplopia* appeared on looking laterally, in many cases already in an eye position deviating only little from the middle. On covering one eye the crossed image disappeared, it was lack of convergence then, evoked or increased by lateral gaze.

A number of them (21) had praenystagmus. Much more frequently there were eye movements as described under nystagmoid. In several severe cases there were eye movements without any regularity and without slow phase from the extreme position backwards; this movement was jerky as well. They were considered as a kind of un- or subconscious eye movement, protecting the patient from the unpleasant concomitant sensations, on a par with closing the eyes and winking.

Some patients at first could not follow a finger more than a little distance from the straight ahead position. With insistence, however, the eyes could follow a finger further, and nearly always the extreme position could be reached for a moment, though it was immediately abandoned again. Such marked objective weakness mostly was accompanied by unpleasant sensations, but not necessarily so. Of the 160 group 89 had weakness of lateral gaze, of these 35 had nystagmus. It may again be mentioned that the number with praenystagmus and nystagmus varied in the course of time in different examinations, this was the incidence at the first examination.

5. Hertwig-Magendie's deviation

In two cases with keen vision, showing a nystagmus in both lateral eye positions, the right eye was observed to turn upwards in looking to the left. The vertical deviation amounted to about 4 mm. This was accompanied by diplopia, the two images being displaced in two dimensions, more vertically than laterally so. One of them had severe weakness of lateral gaze (case no. 133), the other slightly only. All movements on the right eye were normally possible on covering the left one. Thus we were led to believe these two cases to be examples of the rarely encountered *Hertwig-Magendie's deviation*; only manifesting itself in lateral eye position. (See Aubry [4]: Jayle.)

Aubry[4] distinguishes three sets of fibres in the posterior longitudinal bundles:

1. The *horizontal pathway*; serving horizontal eye movements.
2. The *vertical pathway* for eye movements in the sagittal plane.
3. The *rotatory pathway* for eye movements in the frontal plane (rotatory movements).

In destructive disturbances in the first two pathways there may, rarely, occur conjugate deviation of the eyes, lateral and vertical respectively. In increasing disturbance a paralysis of gaze in the direction opposite to the deviation may result; with decrease of the affection a nystagmus in the direction opposite to the conjugate deviation, i. e. slow phase in the same direction.

Example: destructive lesion of the right posterior longitudinal bundle may bring about:

a. *paralysis of lateral gaze* to the right;

b. *conjugate deviation* to the left;

c. *horizontal nystagmus* to the right (i. e. slow phase to the left).

The first is the most marked, the last the slightest form. The slow, essential, phase of the nystagmus is analogous with the deviation. More than that, it is the conjugate deviation in embryo.

Now in lesions of the rotatory pathway:

a. the paralysis does not exist, the rotatory eye movements being purely reflex in human beings. They may be traced, however, by testing for *counter-rotation*, a compensatory rotatory eye movement normally evoked by inclining the head in the frontal plane (*"Gegenrollung"*); our patients were not tested for this.

b. The conjugate deviation is very rarely observed in the form of *Hertwig-Magendie's deviation*, it may then be called *rotatory conjugate deviation.*

c. Rotatory nystagmus is the only objective disturbance to be commonly observed as clinical evidence of disturbances of this pathway in humans[4].

This hypothesis is quite attractive in its simplicity. The question whether these fibres belong to the cortico-mesencephalic, to the vestibulo-mesencephalic tract, or to both, is not considered.

Aubry states that Hertwig-Magendie's deviation may occur in lesions of the posterior longitudinal bundle; rostrally in the mesencephalon, and caudally in the neighbourhood of the vestibular nuclei[4].

Klestadt considers the Hertwig-Magendie deviation to be a "vestibulostatic reflex". Such deviation was seen by Cavius and Russel Brain after therapeutic section of the eighth nerve, accompanied by rotatory nystagmus to the other side. However, all other cases were observed in central lesions[55].

6. Weakness of convergence and accommodation

Weakness of convergence was observed in 74 cases out of 160, sometimes so marked that objects at more than one meter distance could not be seen singly, sometimes in slight degree only. The same subjective sensations as described in lateral eye movements were frequently brought about by attempts to converge, only less so with regard to dizziness. Reading, playing chess, lighting a cigarette and testing for converging power produced such effects. Nystagmus on converging was never observed. Of these 74 cases 38 showed nystagmus as well.

Graefe's symptom (as in hyperthyreoidism) was consistently negative, as was Stellwag's; winking rather being more frequent, especially so on lateral eye movements.

Comment

The centre for convergence is not yet known, however, it is assumed by many writers to be in Perlia's nucleus in the mesencephalon. There is agreement as to its location in the brain stem and corticalwards from the extraocular eye muscles (supranuclear).

Conjugate eye movements, notably lateral gaze and convergence, were very liable to evoke dizziness, sometimes a definite attack. Resting the eyes often caused dizziness to decrease or disappear. Interesting in this respect is Uter-

möhlen's [138] observation, that alleviation of convergence by the use of prismatic glasses relieves or cures the dizziness in Ménière's syndrome.

7. Other conjugate eye movements

Upward gaze was less often and less markedly disturbed than the eye movements discussed above, downward gaze still less so. In upward gaze there sometimes were the same subjective sensations as in lateral gaze, but again of lesser degree. Twice a horizontal fine oscillatory nystagmus was seen in upward gaze.

8. General remarks on conjugate eye movements

The weakness of lateral gaze and still more so that of convergence showed a much more constant character than the nystagmus, which was often varying in existence. Disturbances in these movements frequently were observed in patients with keen eyesight and without scotomata; impaired vision thus could play no role. Resulting from this weakness of lateral gaze and of convergence, possibly also from blurred vision (see ophthalmic findings) these patients tended to fix their eyes centrally in the orbits. The often extremely unpleasant sensations elicited by movements of the eyes caused them to be very careful in this respect. One and the other resulted in a most *peculiar, staring, lifeless gaze*, which several patients showed as early as in the second year of captivity. This kind of gaze is consistently described in pellagra [74, 85, 11, 140] etc.

Hypokinesia of the mimic musculature might contribute also to this characteristic expression, although I doubt this because of the abovementioned normal or increased frequency of winking. It must be admitted, however, that no special attention was paid to the frequency of winking in some cases with very marked staring gaze. This is the more to be regretted because there was another symptom, which might be dependent upon lesions of the basal ganglia and which was not rated at its full importance during the investigation. Statistics cannot therefore be given.

When following a slowly leading finger, not infrequently in these patients both eyes momentarily halted, as if they encountered some inflexible obstacle, which, however, was breakable. The eyes then, immediately after this halt, overtook and followed the finger again. This phenomenon might appear 2—3 times in a sweep from one lateral position to the other, and occurred in some 20—30 % of patients. It was never observed in patients who did not show the oto-neurological syndrome described now, so that, when testing for first degree nystagmus on the first eye movement from the middle position lateralwards due suspicion was aroused when this phenomenon was observed.

Comment

This phenomenon is identical with that described by Bielschowsky as "*Sakkadierung*", perhaps best translated as "saccaded". These *saccaded eye movements* are called *ocular cogwheel phenomenon* by Bing, because of the resemblance with Negro's cogwheel sign in the limbs in paralysis agitans and epidemic encephalitis [12]. It depends upon disturbance in the „decontraction" of the antagonists, which always accompanies contraction of a group of muscles by reciprocal innervation (Sherrington) [13].

Saccaded eye movements are described by Bielschowsky in disturbances of the extrapyramidal motor system. In these disturbances there is discrepancy between eye movements on command without object of fixation, and those while following a moving object. The former are poor, the latter normal in extent, but sometimes saccaded [12].

Unfortunately these patients were not systemetically tested as to free eye movements on command, as contrasted with those while following a moving object. It is a pity that also insufficient attention was paid to low frequency of winking, because the lifeless, staring look as well as the saccaded eye movements might depend upon lesions of the basal ganglia, which again are found post mortem in pellagra and in central neuritis [74] (see below). Nevertheless, basal ganglionic lesions being the cause of these phenomena is doubted because for the following reasons:

1. Few confirmatory neurological signs were found (see neurological examination).

In Pakan Baroe however, one patient was seen who for weeks showed a hyperkinesia of all four limbs. He was paretic, could hardly walk, but was moving his arms and legs all the time, even when sleeping, slowly, with little jerks, assuming the most peculiar positions. This disappeared completely. A few months later he died after delirium and coma lasting some hours. Post mortem there was excess of fluid in the ventricles and outside of the brain, with slight atrophy of cerebral substance (Verhaart, L. Simons). Basal ganglia and other parts of the brain were macroscopically normal on multiple sections. (No record available.)

2. In many patients frequent winking was observed, especially in looking laterally.

3. No discrepancy was found between eye movements on command and those while looking at a moving object, though the former were not consistently tested for. There was often extreme difficulty in following a finger to the lateral position.

4. Bielschowsky states that in these extrapyramidal motor lesions, once the lateral direction of the eyes is reached by following a moving object, the eyes tend to stay on this object [12]. This was never so in our cases. They tended to let it go as soon as possible.

Bielschowsky further mentions Cantonnet who in locomotor ataxia (tabes dorsalis) describes one patient with apparently the same phenomenon. It is brought under the heading "Ataxia of the eye movements" now, because several writers mention ataxia of the eye movements (in other forms) in locomotor ataxia, analogous to other ataxic disturbances in this disease [19].

9. Ataxia of the eye movements

In 6 patients difficulty was observed in following a finger from, let us say, 1½ meter to 20 cm. distance (record no. 30). Now the degree of convergence was too big, now again too small. Only in the moment of crossing was it momentarily correct. Sometimes convergence became so marked, that it could be called a momentary spasm, which was immediately relieved by letting the eyes go to parallel gaze. Mostly dizziness resulted with convulsive closing of the eyelids. When the finger was stationary they managed after some effort to fix it binocularly; when the distance was altered, the ataxic movements started again. This phenomenon was called *ataxia of the eye movements*, perhaps better *ataxia of convergence*, because it was never observed in conjugate movements other than convergence.

It is believed that this difficulty in fusing the two retinal images was present in many patients, and that partly this was responsible for complaints of diplopia. (This complaint certainly was partly dependent upon weakness of convergence). This disturbance in fusing then, being probably present in many cases, was in the more severe forms to be demonstrated by aggravating the demand; in this case by changing the distance of an object from the eyes.

In the Bandoeng camp it was possible to play baseball. Several players complained of difficulty in judging the distance of an oncoming ball, whereas formerly they never experienced this. These slightly imbalanced ocular movements constitute a very early symptom of the disease then. I experienced this difficulty in estimating distance myself. Occasionally I observed diplopia as well in myself. This is a queer sensation. One at first thinks that there are really two objects, but at times from the type of object or from previous experience, this is patently absurd. It is a very strange sensation having difficulty in fusing the two images. I did it by consciously increasing and decreasing convergence by „climbing" along objects on gradually decreasing or increasing distances, for example, along the floor.

Comment

Apart from the abovementioned case of Cantonnet, Bielschowsky mentions under the heading "Ataxia of the eye movements" cases of convergence spasm occurring on attempts to carry out eye movements on command, i. e. while not following a moving object. This was only observed by others, in locomotor ataxia, never by Bielschowsky himself; he doubts the value and significance of the symptom. In following an object moved in different directions there was no difficulty [12].

These disturbances in eye movements on command were never observed in our patients, although they were not consistently tested for this. Frostig and Spies [89] describe as psychical disturbances in pellagra fear that collisions will occur when the patients are watching busy traffic. Of course the pessimistic mind often observed in pellagrins may play an

important part; however, this ataxia in convergence may considerably decrease their power to estimate distance and account for the fear for collisions. Several onlookers in baseball experienced the same fear when two running players closely passed each other. With regard to the intricate play of eye movements, proprioceptive impulses provided by them, and retinal images, which make the evaluation of small differences in distance possible for normal people, these patients are considerably and early harmed.

The above mentioned case of Cantonnet is not available to me in the original article. As Bielschowsky describes it, it is closely resembling Bing's extraocular cogwheel sign. In this case it was observed in following a moving object [12].

10. Anisocoria and other anomalies of the pupils

Anisocoria was observed in 31 out of 160 patients. Most often it became evident in dull light only, the difference becoming much smaller or even imperceptible in bright light. This anisocoria might be varying in degree and in existence; occasionally the bigger pupil might be found shifted from one side to the other. Subjective complaints herefrom were never observed.

A few cases were observed with *irregular pupils* on one or both sides, without iritis or other ocular inflammation in their history. In all cases with anomalies in form of the pupils the M(einicke) T(rübungs) R(eaktion) was done (Ten Seldam), but it was consistently negative. In a few cases lumbar puncture was performed, which revealed apparently normal pressure and also no abnormalities as to cell- or protein-contents. The M.T.R. was negative in this fluid as well (Ten Seldam). The pupils always reacted to light and convergence, directly and consensually. If convergence was weak, the pupillary reaction to convergence of course was proportionally lowered.

There were several patients with conspicuously large pupils. No agreement as to this could be obtained with the ophthalmologist (Schwartz). His opinion was that pupils might range considerably in size within normal limits. Since, however,

there were frequent complaints of photophobia, and several patients showed conspicuously wide pupils, *mydriasis* as a possible cause for the complaints was considered in several case reports. Photophobia certainly might be dependent on bulbar conjunctivitis and peripheral keratitis caused by ariboflavinosis.

Comment

Lewy, Spies and Aring describe anisocoria, other form anomalies of the pupils and mydriasis in pellagrins in their publication, previously mentioned (1940). Mydriasis was determined by careful measuring [70]. This symptom, moreover, is mentioned by Manson Bahr [74] and others in pellagra.

11. Hearing

Of this group of 160 patients 33 had normal hearing, as judged by the methods of examination available. Of these, 23 had a nystagmus, 6 a praenystagmus.

Owing to the very poor equipment for hearing tests, it was difficult to determine what type of deafness was present, however, this was done as best as possible on the generally accepted principles. Reduced bone conduction, negative Rinne, deafness in the higher tone range covered by whisper were thus considered as indicative of perception deafness; lengthened or relatively little decreased bone conduction in considerable hearing loss, and deafness more marked in the lower tone ranges as signs of conduction deafness. Weber lateralized to the most deaf ear as disturbance in conduction, and vice versa.

Reasoning thus, the 160 patients were divided as follows:

Normal hearing	33
Deafness of conduction type ...	19
Deafness of mixed type	15
Deafness of perceptive type	93
total....	160

Of the 19 patients with conduction deafness 10 had nystagmus. Of the 93 cases with hearing loss of perceptive type there

were 42 with slight loss only, hearing being diminished only for some whispered words to 4 meters at the most and the bone conduction only slightly reduced.

In 49 the perception deafness was more marked, up to considerable hearing loss in several cases. Among the patients with perception deafness there were many in whom hearing loss might be due to an obvious causative factor, like quinine, machine gunning, driving aeroplanes and armoured cars, nicotine abuse, etc. Also some cases which were already deaf before captivity and (or) had a family history of presbyacusis or juvenile nerve degeneration, were brought into this group. Especially from the group with slight hearing loss a considerable number could be subtracted in this way. It should be borne in mind, however, that also for this number with obvious reasons for their hearing loss, a deficiency might have been responsible, alone, or in addition to the other cause.

In any case, reasoning thus, there remained 30 people with considerable and 12 with slight hearing loss of perception type who became deaf in the camp without an obvious cause in their previous history. For these deficiency was assumed to be the cause. In addition there were 2 cases of mixed deafness of which the perceptive part was considered to be caused by deficiency. Bruining was, so far I know, the first in our camps to recognize this sort of deafness, in Tjimahi Hospital, 1943. This loss in hearing power might progress rapidly and markedly (see for instance case mentioned under subjective hearing loss). On the whole, however, it was a slow and nearly imperceptible process, of which the patients themselves often were not aware. In nearly all cases the deafness was bilateral, although there might be slight differences between the right and the left ear. Of this group of 42 patients with deficiency deafness, 23 had weakness of convergence, 21 nystagmus and 14 both.

Comment

Conspicuous is the high incidence of nystagmus in people with normal hearing (23 in 33) and in patients with conduction deafness (10 in 19), in contrast to only 11 patients with deficiency deafness showing nystagmus out of 42. The deafness

of perception type nearly always being bilateral, a central cause for the deafness is not impossible.

Discrepancy between hearing loss for the human voice and such for tones as positively centrally pointing findings (De Kleyn[62], Güttich[46], de Crinis[24]) could not be tested for owing to lack of equipment.

De Kleyn describes 21 cases with acute destructive disorder of one or both acoustic systems in Holland. By far the greatest number were observed in 1941 and '42, so that the author considered the possibility of avitaminosis; but the B_1 and nicotinic acid level in the blood were normal[62]. However, in pellagra the nicotinic acid blood level is as a rule not lowered (Querido et al.[6, 94]; Field, Melnick et al.[36]); riboflavin and pyridoxin could not be tested for. Both nicotinic acid and (or) riboflavin may have played a part. Especially so, because de Kleyn assumed central lesions in the majority of his cases[62]. In parenthesis, the same reasoning applies to some cases of acute oesophagitis and some of submucous haemorrhages of the pharynx, observed by de Kleyn in war time[63].

Selfridge is, as far as I know, the first who consciously and thoroughly contemplated the possibility of deficiency causing nerve deafness, and treated cases along these lines. Covell and he produced demyelinization of both branches of the eighth nerve in rats and chicks fed on a diet deficient in different factors of the B complex, B_1, B_2 and especially the filtrate factor[109]. In a second paper Selfridge attributes more importance to nicotinic acid[110]. So far I can see, no oto-neurological vestibular examination was performed in his cases to determine the site of the lesion, whether central, peripheral or both. In the third publication[111] B_1 is added with further results. This author through many years of labour and experiments arrives at the conclusion that lack of several factors of the B complex may bring about nerve deafness, the reverse being true as well[111].

Querido mentions deafness in pellagra[94]; also Manson Bahr in central neuritis and in connection with burning feet[74]. In Jamaica deafness was frequently noted in „central neuritis", by Scott, Strachan and others[107]. Bick-

nell and Prescott report a publication from Covian and Garcia on perception deafness after malnutrition in the Spanish civil war, accompanied by glossitis, cheilosis, loss of visual acuity, paraesthesiae, a burning pain in the soles of the feet and ataxia [11]. Burgess noted deafness in allied prisoners of war at Changi camp, Singapore, in 1942—1945 [18], among many other symptoms.

There are more publications on the subject. Deafness caused by deficiency is a little known fact, most of the text- and handbooks on otology and neurology do not even mention it; if they do, they are more or less sceptical. The same appertains generally to nystagmus. These symptoms are insidious ones and easily masked by many more annoying and more conspicuous symptoms. This is already so in the initial stage of pellagra, more so in the latter stages, when many life threatening symptoms demand all attention from both physician and patient. I had the dubious pleasure of witnessing this personally. As to the hearing, the patients themselves are often unaware of their disability, which may be slight and generally developes so slowly. Often they are surrounded by people in the same condition and therefore the trouble passes unnoticed. Finally, only rarely the deafness is so marked as to be annoying.

12. Romberg test

This test was always done in the classical manner, with feet close together and eyes closed. No sensitized Romberg in other foot positions was taken.

This test was positive 19 times, 4 times dependent on head position and 15 times independent thereof. In these last instances the patients often fell backwards, or backwards and laterally, in an oblique direction. In the 4 cases the Romberg test was positive in a direction dependent on head position (case no. 19 backward), there were other symptoms which pointed to the central area, like hyperirritability, dysharmony with the walking and pointing test, etc. (no. 86, 93, 130). Considering all the 19 positive Romberg cases, there were none with a clearly cut, harmonic peripheral picture (see table and comment on pointing tests).

In the same patient the direction of falling mostly remained constant in the course of time, in different individuals the direction of falling varied. In 41 further cases there was swaying of abnormal degree, although falling could be avoided. When the eyes were opened, there was always a marked improvement, mostly all symptoms disappeared; this also occurred in the 19 positive cases.

Comment

The positive Romberg in a fixed direction, independent of position of the head, as well as the falling occurring in a plane other than the frontal one, are symptoms pointing to the central vestibular area (Aubry [4], Klestadt [55], Ballenger [5], Burger [17], Bing [13], Wechsler [142] and many others). Lewy et al. observed rombergism in their neurological examination of pellagrins [70], Castellani, Chalmers [20] and Manson Bahr also. The latter mentions a peculiar tendency to fall backward [74].

13. Walking test

In 74 cases the findings in this test were not normal, 39 of them swerving to both sides. In 14 cases there was marked *ataxia*: 3 patients fell repeatedly, though they could walk quite well with eyes open. In 35 there was a definite deviation in one direction, which remained constant in the same patient in the course of time, although there might be quantitative variations.

14. Pointing tests

In horizontal deviations only those exceeding 5 cm. were taken into consideration, in deviations downward only those in excess of 10 cm. Upward deviations were never seen.

Spontaneous abnormalities in pointing occurred in 57 cases. In most of them deviations exceeded 10 cm.; pointing was nearly always faulty in the vertical plane, vertical deviations being rare. The distribution was as follows:

a. *Irregular deviations*, being to the right and to the left, rarely up- and downward, mostly with both arms, giving the

impression more of incoordination than of a systematized deviation. This concerned 27 cases, of which 25 were bilateral and 2 unilateral. One case showed marked ataxia of all movements of the body.

b. *Outward deviation*, of constant character, in total 24 cases, of which 19 unilateral and 5 on both arms.

c. *Past pointing with both arms to the same side*, in 4 cases.

d. *Downward deviation* (exceeding 10 cm.) in 2 patients.

Comment

In only a few cases was there harmony between the slow phase of nystagmus, past pointing, walking deviation and direction of positive Romberg. Direction of Romberg and walking deviation went hand in hand in slightly more cases. There was often *vestibular dysharmony* then, by which is meant that there is discordance between slow nystagmus phase, past pointing, deviation in the walking test and direction of positive Romberg with head in normal position. The slow nystagmus phase is the same movement in the eyes as the deviation is in other parts of the body. This vestibular dysharmony is a characteristic sign of affection of the central vestibular area, whereas in peripheral lesions there is strict vestibular harmony (Aubry[4], Klestadt[55], Ballenger[5], Burger[17], Bing[13] and many others). All authors agree on this point, so far I know. On the whole spontaneous past pointing, and still more so a positive Romberg test, are less suited for localization than other vestibular symptoms [55,4], and only to be counted when they are constant and accompanied by other symptoms of the vestibular system [55].

Aubry states that past pointing, when central, is most often unilateral and may be harmonic or dysharmonic. It may be evoked anywhere in the central vestibular pathways, but most often in or near the nuclear area. He considers it to be a sign of irritation; when unilateral, the lesion is on the homolateral side and the deviation goes mostly outward. Vertical deviations are more rare. Spontaneous past pointing, when peripheral, on the whole concerns both arms, though

the arm homolateral with the lesion often is influenced to a greater extent. The past pointing is in harmony with other spontaneous vestibular symptoms [4].

There were in our material 19 unilateral and 5 bilateral spontaneous outward deviations. In each of the 4 patients showing bilateral past pointing in one lateral direction there was dysharmony either with the walking, or with the Romberg test, or with both; and in addition there were other centrally pointing symptoms (see case no. 14, and table no. 5, 74 and 95).

Regarding the pointing tests on the whole, and in comparison with the walking and Romberg test, we may conclude that there were many central symptoms, and no peripheral vestibular syndromes in the cases where pointing was spontaneously abnormal.

15. Caloric (cold) stimulation

More than ¾ of the 160 patients (118) were *hyperirritable*, with quotients of 7 or more (Atkinson [2]), up to 15 and 20. Subjective sensations in most cases ran parallel with the quotients, although in some cases with high quotients there was some proportional lagging of the subjective sensations. Among the very high quotients patients with exceedingly unpleasant reactions were observed, such as sudden, rigid falling to the irritated side, profuse sweating, vomiting, occasionally even diarrhea and fainting. In such cases only one ear was tested, for obvious reasons from both the observer's and the patients' point of view. Many hyperirritable patients for 24 hours or more after vestibular examination felt abnormal or more ill than before. With repeated observations, when mostly only the eye movements were tested, this same aggravation of their complaints was reported, only to a less degree and mostly of shorter duration.

Spontaneous nystagmus was temporarily abolished by nystagmus in the opposite direction induced by Atkinson's method. On the whole it may be stated that induced past pointing was not, or little marked; in some cases with great liability to nystagmus and subjective sensations it failed to occur. Insufficient attention was paid to this phenomenon, so

that I can give only a general impression. The induced Romberg generally was more in harmony with the abovementioned reactions. Finally there were a considerable number of patients with hypoexcitability of the rotatory pathway, to be discussed seperately below. The hyperirritability mostly was found in both ears, though there might be slight differences between right and left in the same patient. Summing up, it may be stated that the excitability to cold stimulation, in order of intensity, was in general as follows:

1. Atkinson's quotient (duration of induced nystagmus over latency).
2. Subjective sensations (vertigo, sweating, nausea, falling, fainting, diarrhea).
3. Positive Romberg.
4. Past pointing.
5. Rotatory nystagmus.

Of course induced phenomena only are meant, or increase (respectively decrease) of spontaneously existing signs by cold stimulation. Klestadt and others demand for the diagnosis "hyperexcitability" spontaneous symptoms, like vertigo or nystagmus [55]. In nearly all of our patients one or the other was present. In a few patients turning tests were done, in these cases excitability on turning paralleled that on cold stimulation. Unfortunately this could not be done consistently, nor could galvanic stimulation for aforementioned reasons. When speaking of hyperirritability, only that on cold stimulation is meant.

Comment

This hyperexcitability was the most consistent symptom of all (118 of 160). Next came vertigo in some form (101) and burning hands and feet (101). That is to say, hearing loss is left out here (127 of 160), because only for 42 cases deficiency was highly probable as the sole or chief cause. Of course it must be borne in mind that this group of patients was selected from a malnourished camp population because of vertigo, deafness, headache, ataxia etc. Viewing the same population as a whole, burning hands and feet, sore mouth and retrobulbar neuritis showed the highest incidence, ranging approximately

from 5—700 of a total strength of 6000. What I wish to make clear is that in this "oto-neurological" group of 160 patients hyperexcitability was the most consistent symptom, and this especially with regard to horizontal nystagmus and subjective sensations.

This hyperexcitability persisted throughout the 9 months (March—December '43), that I carried out caloric cold stimulation. Unfortunately in Batavia this was not possible either for Bruining or for me; still less so in Pakan Baroe. Kuilman [65, 66], in Batavia, more than six months after I did the last vestibular tests of any quantitative value, found normal excitability to temperature and turning (Batavia, June 1944—1945). I am not aware how he tested them. Kuilman was bound to see several of the same patients I observed earlier. Assuming that our findings are comparable, a possible explanation may be the following: My findings were hyperirritability, Kuilman's, a considerable time later, normal irritability, while the subjective complaints and objective symptoms had remained the same, even strikingly so. Mohr [78] (see under ophthalmic findings) in early stages found a hyperaemia and oedema in the optic discs, the macula lutea and the retina. Later pallor preponderated; oedema, hyperaemia and small haemorrhages disappearing. Schwartz [106] in our group of 160 patients, found 9 patients with hyperaemic discs and normal eyesight, more than one year after Mohr's initial findings (Sourabaia). Here negative findings preponderated, next came disc pallor; hyperaemic discs occurred rarely. Schwartz postulated the probability that these hyperaemic findings were initial ones. The retina being part of the brain, it is quite possible that in the brain stem the same changes are present, in the same order of sequence. It is quite possible then, that in 1943 there was hyperexcitability with hyperaemia of the central vestibular area, while Kuilman in the latter half of 1944 and in 1945 found normal irritability in a central vestibular area presenting no hyperaemia but normal capillary width. The complaint may remain with changing conditions in the central vestibular area, passing from hyperaemia to anaemia on the whole, but with many temporary fluctuations giving rise to

subjective and objective spontaneous symptoms. As long as the process exists, central vestibular disturbances are apt to produce subjective and objective disturbances (K l e s t a d t [55]). This will account for the long standing nature of the vestibular symptoms in our patients, which in itself is a sign of involvement of the central vestibular area ((A u b r y [4]).

In trying to explain the discrepancy between K u i l m a n's and my findings we have encroached upon the localization of the lesions. It will have come to the mind that in the symptomatology described up to now there were many symptoms pointing to the brain stem, and few to the peripheral vestibular area. The hyperexcitability in itself, in the consistent absence of otoscopic findings of inflammation, and in its lasting character (several cases were controlled for 9 months by me) is a typical central symptom, according to K l e s t a d t. When found in both ears, as was mostly the case in our patients, it is met with in neurasthenia and in infants; also in encephalitis and disseminated sclerosis, and generally in affections of the central nervous system liable to remissions and exacerbations [55]. Now pellagra is a typical disease running such a course with periodical exacerbations, and affecting the central nervous system (see below).

Group forming in induced nystagmus was never noted. At the time of investigation my knowledge on the matter was not such as to include this phenomenon in disturbances in nervous fibres afferent to the nuclei of the extraocular eye muscles. The observation of this phenomenon in spontaneous nystagmus (which at the time, because of irregularity, was brought under "nystagmoid") was only valued much later, when more literature on the subject was available (D e K l e y n [59], K l e s t a d t [55], F r e n z e l [38], A u b r y [4], etc.). This is the reason why I am not able to give figures on group forming in spontaneous nystagmus, out of this group "nystagmoid", in which other forms also were included. In cases with spontaneous nystagmus or "nystagmoid" the eyes during caloric tests were watched in a position, free of spontaneous movements, more towards the central position. So far I can remember and recollect from the case reports, there was always a regular induced nystagmus at the outset; often towards the

end of its period of duration, however, it became irregular, and this moment was taken for expiration, the excursions at that time always being very small. This was done so as to avoid obtaining a too long time of duration, especially when spontaneous eye movements in lateral positions were present; in other words, to remain on the safe side. Notwithstanding this line of conduct, A t k i n s o n's quotients were high enough on the whole. No particulars other than horizontal or rotatory or both were recorded in induced nystagmus; so unfortunately I cannot give an opinion on induced nystagmus, as to group forming.

It is opportune here to consider another phenomenon not known to me at the time of captivity: the *abolition of the quick phase in induced nystagmus* (on slight stimulus). There were a few patients, alluded to above in the symptomatology of induced nystagmus, who fell like a rigid pole from a sitting position to the stimulated side. They closed their eyes convulsively, two fainted, one got diarrhea. I remember quite distinctly one having a conjugate deviation of the eyes, no nystagmus, immediately after the onset of the reaction. Not knowing the symptom, I paid no special attention to this, being more concerned with the alarming other reactions. No further labyrinthine tests were carried out in such patients. I cannot remember towards which side the deviation occurred; in the other cases I did not look at the eyes.

Summing up it must unfortunately be stated that definite observation is not available on either group forming in induced nystagmus, or on abolition of the quick phase therein.

16. Eagleton's symptom

This was described by E a g l e t o n in 1923; and earlier, in 1918, by F i s h e r and J o n e s, according to K l e s t a d t [55]. It consists of *hypo-irritability of the pathway for rotatory nystagmus*. F i s h e r, J o n e s and G r a n t consider the symptom already significant in marked hypo-excitability for caloric stimulation (according to K l e s t a d t [55]); A u b r y [4] demands inexcitability for all three methods of stimulation, and especially for galvanic irritation,

because this method normally always brings about rotatory nystagmus.

In our patients only caloric stimulation was done. In 26 cases there was no rotatory component to be obtained in a head position 60° backwards and 45° to the unirritated side. Then only horizontal nystagmus showed itself. The same occurred in head position 30° forward; in most cases the horizontal nystagmus then disappeared completely or had a very small amplitude. On shifting the head to 60° backwards a marked horizontal nystagmus could be obtained again. It goes without saying that all these positions were not tried successively in one patient, new forms of nystagmus taking too long to establish for the duration of the induced nystagmus. However, as stated above, the position 60° backwards and 45° to the other side was always tested; after having met some positive Eagletons, observation was started in this position after clearing the external canal.

Of these 26 cases 15 were positive on one, and 11 on both sides. Further there were several more cases in which the rotatory component of induced nystagmus was very weak in the optimum position for the vertical canals; these were not calculated. In some less irritable cases the test was repeated with 100 c.c. icewater, slowly injected, without obtaining rotatory nystagmus.

Summing up, there were 26 cases which failed to show rotatory nystagmus on caloric stimulation, 15 unilateral, 11 bilateral. Most of them were hyperirritable as to horizontal nystagmus and subjective sensations.

Comment

There is general agreement that Eagleton's symptom depends on intrapontine lesion (Wechsler[142], Bing[13], Klestadt[55], Aubry[4] and others). There is controversy as to the significance of the symptom, whether unirritable or hypoirritable; whether on merely one method of stimulation, or in the impossibility of eliciting the rotatory nystagmus, all known methods being used (see above). According to Aubry Eagleton's symptom is elicited by a lesion in

the posterior longitudinal bundle, between the vestibular nuclei and the posterior commissure[4].

17. Abnormalities of past pointing and of rombergism on caloric stimulation

a. With Atkinson's method of stimulation in 25 cases a *reactive outward deviation of the contralateral arm* was noted. In all pointing tests only deviations larger than 5 cm. were taken into consideration. This symptom was present on one side in 19 and on both sides in 6 cases. Wechsler[142] and Bing[13] explain this as a disturbance of the cerebellum or its pathways.

b. In 11 patients past pointing failed to occur, whereas nystagmus and rombergism were normally evoked, in 7 on one and in 5 on both ears. This again is interpreted by Wechsler[142] and Bing[13] as disturbance in the cerebellum or its pathways. The abolition of one or the other component of the reactive vestibular phenomena is called *dissociation*, the name was given by Cambrelin[96].

c. In 3 patients a positive Romberg was evoked in a direction other than to the stimulated ear. They fell backward.

d. In 2 cases definite spontaneous past pointing disappeared after cold water stimulation, which Barany interprets as cerebellar irritation being the cause of the spontaneous past pointing[142, 13].

e. In one case cold stimulation of the right ear gave past pointing of both arms to the left.

In total 37 patients showed one of the abovementioned forms of dysharmony; a few patients showed more than one of these abnormal reactions then.

Comment

In peripheral vestibular lesions there is vestibular harmony, in central disturbance there may be vestibular dysharmony, spontaneous as well as reactive. All authors agree to this fact. However, there is no agreement as to the exact site of the lesion in different forms of this dysharmony. Klestadt

mentions among others the opinion of Barré and Klein, formed on 20 cases, in which the direction of reactive movements of the body or limbs were dysharmonic with the slow nystagmus phase. They assumed a lesion of the floor of the 4th ventricle, especially by pressure from the cerebellum [55].

Aubry considers as the most reliable central sign of the reactions under discussion, a positive Romberg which cannot be altered by vestibular irritation [4]. This phenomenon was observed in 3 cases with spontaneously positive Romberg, one dependent on head position (no. 130), two independent thereof (no. 140 and 156). However, irritation was not performed with larger quantities of water, but with 1 c.c. 0° C (Atkinson) there was no alteration whatsoever of the direction of spontaneous falling, while nystagmus was elicited in great intensity and duration.

Güttich regards absent induced past pointing as a retrolabyrinthine lesion. In lues it is reported in 75 % of all cases, in which it is said to be caused by leptomeningitis, affecting the VIIIth nerve (peripheral); others consider it to be a central symptom, evoked by disturbance either in the vestibular nuclear area, or in the vestibulospinal tract, or in pathways coursing through the cerebellum [55]. Syphilis in our patients could be put out of court by blood reactions and for other reasons.

According to Aubry, Hautant considers the symptom to be one of the first signs of diminished activity of the vestibular system [4]. If this is true, a lesion of an intensity giving rise to abolition of reactive past pointing, could cause irritation of more resistent systems, according to generally prevailing physiological laws. The same applies to the rotatory nystagmus with regard to the other nystagmus forms. In this way the discrepancy may be explained between abolished reactive past pointing (and rotatory nystagmus in other cases), and exaggeration of other induced vestibular symptoms.

Aubry states that whereas spontaneous past pointing may be elicited anywhere in the vestibular area, abnormalities in induced past pointing, if central, are rarely seen but in lesions in or caudally from the vestibular nuclear area [4].

Vestibular dysharmonies and dissociations are explained as

central by most authors [55, 4]. From an anatomical point of view this is necessary, because in the labyrinth and vestibular nerve always either all or none of the vestibular components will be affected. In the brain stem, where the different sets of fibres split up, isolated lesions are more readily possible. However, often a greater vulnerability of one component of the vestibular system has to be assumed to explain an isolated abolition, and with regard to this a peripheral site might be equally possible. Thus also in these cases we have mainly or exclusively to rest upon pathological findings in clinically known patients, and afterwards to search for some theoretical explanation.

Eagleton's symptom is also such a dissociation.

Summary

Hyperexcitability of the labyrinths (by cold water) was the most consistent symptom (118 of 160). Then followed nystagmus with 94 cases; praenystagmus was observed in 48 cases. The most common form of nystagmus was horizontal bilateral. Weakness of lateral gaze was seen in 89, weakness of convergence in 70, and nystagmoid eye movements in 67 patients, part of the latter showed group forming. Spontaneous abnormalities in the walking test were observed in 74, in the Romberg test in 60 and in the pointing test in 57 cases. Hearing loss of perceptive type and due to deficiency was noted in 42 patients. Only 33 patients had normal hearing acuity, but in most of the others occupational causes might be held responsible for slight hearing loss of perceptive type (soldiers). Reactive vestibular dysharmony or dissociation was met with in 37, Eagleton's symptom in 26 cases. Anisocoria was present in 31 cases, mydriasis frequently, irregularity of the pupils occasionally.

Bing's ocular cogwheel phenomenon was frequently observed, further a few cases of ataxia of convergence movements and 2 cases of Hertwig-Magendie's deviation. The typical, lifeless, staring gaze of pellagrins was not infrequently observed in marked form as early as in Bandoeng (1943).

18. Neurological examination

This was performed by Buitelaar† and Van der Hoeven† on the group of 160 patients at Bandoeng. Since both died, only main findings very briefly entered into my sick-reports are available. Of course partially the same symptoms observed in the oto-neurological examination described above, were reported again by them; to avoid repetition, we will only mention phenomena, not discussed as yet.

In 25 cases there were disturbances in the *finger-finger, finger-nose,* and *heel-knee test,* or other forms of *ataxia,* from which as such it was impossible to conclude whether they resulted from affection of the peripheral nerves, of the spinal cord, or of the brain stem.

An- or *hypaesthesia* in the area of a *peripheral nerve* was found in 8, of *sock-* or *glove type* in 7 cases. Of the peripheral nerves the peroneal was most commonly affected. In some other patients there were disturbances in deep sensation of such distribution, that central nervous lesion was suspected. This concerned *loss of vibration sense* twice, disturbance in *discrimination* in 4, and in *proprioceptive feeling* in 2 patients.

Cerebellar signs were found in one case only: *disdiadochokinesis* in a patient with outward deviation of the contralateral arm on cold stimulation (no. 40).

The *tendon reflexes* were frequently *exaggerated* (28 cases), much less diminished or absent (6 cases). Tremors were common, but little marked.

In Pakan Baroe Verhaart saw many neurological cases. There the number of cases with *diminished* or *abolished tendon reflexes* were considerable, due to beriberi. One of our Bandoeng nystagmus patients died there, showing a full-blown *Korsakoff syndrome* (record no. 21).

Apart from this group of 160 patients Verhaart and I observed a young British soldier with nearly second grade bilateral horizontal nystagmus, who died paralytic after a delirious period of some days. The diagnosis *Wernicke's encephalopathy* was made by Verhaart and substantiated by the post mortem finding of multiple small haemorrhages,

about half the size of a grain of corn, along the Sylvian aquaeduct. In the same camp further cases of death following cerebral symptoms occurred, the diagnosis of cerebral malaria being excluded by repeated bloodslides and post mortem examination (L. Simons). In the greater part of these cases no lesions were found in the brain macroscopically; in one of them, however, numerous haemorrhages of the same size as those mentioned above were found scattered over the whole surface of the brain; in, or immediately under the pia mater; most dense over the cerebellum. (This patient was not known to show oto-neurological disturbances). Finally, there were a few cases in whom *clouding of consciousness* and *grasping and sucking reflexes* were observed, of which I have no further data (Verhaart).

Comment

The neurological findings in Bandoeng have little characteristic value, they were too little marked on the whole. In beriberi as well as in pellagra exaggerated deep reflexes are common in the beginning [20, 74]. Both diseases affect the whole nervous system, beriberi more the peripheral, pellagra more the central part [74, 11, 51].

In Pakan Baroe both diseases abounded, mixed forms being quite common and to be expected. Jolliffe et al. observed in the course of time 150 cases of "*nicotinic acid deficiency encephalopathy*". This syndrome may occur either as the only clinical manifestation of a deficiency disease, or in association with pellagra, polyneuritis due to B_1 deficiency, the oculomotor disturbances of a central neuritis, or scurvy. The clinical picture is characterized by progressive clouding of consciousness, cogwheel rigidities of the extremities, uncontrollable grasping and sucking reflexes and mostly dehydration. Statistics are as follows:

Treatment	Cases	Mortality (corrected)
House diet + hydration	47	89,4 %
,, ,, + B_1	15	100 %
Vitamin rich diet + vit. B complex	66	51,5 %
Basal diet + hydration + nicotinic acid	22	13,6 % [51]

Further comment on the influence of nicotinic acid seems superfluous. Some cases had a history of alcoholism. Interesting in this respect is, that Bender and Schilder in 1930 described a similar clinical picture in alcoholics [10], that Sydenstricker and Spies observed this syndrome in endemic pellagrins [51] (follow our cases in Pakan Baroe), and that in '41 Stevenson et al. came to the conclusion that probably most of the (relatively slight) post mortem changes in the central nervous system of alcohol addicts are due to avitaminosis rather than to the toxic effect of alcohol itself. The latter found nystagmus in 8 out of 22 cases; of the nystagmus cases 7 had other signs of avitaminosis. Wernicke's and Korsakoff's syndromes were observed [130] (one case of each in Pakan Baroe, without a history of alcoholism).

Central neuritis is a disease seen on sugar estates in Jamaica by Scott in 1918 [107, 74]. Similar conditions were observed elsewhere. It occurred there when the diet consisted mainly of sugar. Cases ceased to occur when the crop was out and disposed of. The symptomatology is the same as in pellagra (including ariboflavinosis), except the "big" dermal symptoms. A scrotal rash is common. Most of the peripheral nerves undergo Waller's degeneration in slight degree, while the posterior root ganglia and the spinal cord, especially the posterior zones, show more marked degenerative changes. The medulla, pons cerebellum, basal ganglia and optic nerves are also severely affected, the VIIIth nerve to a less extent. Deafness is mentioned, vertigo not. An intimate association between this disease and pellagra is noted; Watson assumes this mainly on pathological grounds [74]. Still, it is not called pellagra, apparently because of the absence of the characteristic skin lesions. It is interesting that in Manson's 1945 edition the chapter "Central neuritis" is omitted and a few lines are devoted to this disease under the heading "Pellagra". The name was proposed by Adolf Meyer, who in 1901 found pathologic alterations in the central nervous system of chronic alcoholics and in other psychic disorders. The aim was to contrast the mainly central distribution of this parenchymatous degeneration with (peripheral) polyneuritis [77]. Scott chose the same name for the "epidemic" in Jamaica because

of the close resemblance between his post mortem findings in the central nervous system, and Meyer's [107].

Wernicke considered the syndrome which is bearing his name as of alcoholic aetiology in part of the cases [52, 130]. Stepp and Kühnau considered Wernicke's syndrome as caused by B_1 deficiency in 1939; it is looked upon as a B complex deficiency by Jolliffe et al. in 1941 [52], and by Bicknell and Prescott in 1946 [11]. Grande and Jiménez investigated cases of neuropathy during the civil war in Spain. They found that lactic acid was metabolized normally, concluding that there was no B_1 deficiency. Pellagra was common there, not beriberi. These neuropathies were not cured by B_1 or nicotinic acid, but responded to treatment with yeast [11].

There is a close relation between Korsakoff's and Wernicke's syndrome and Jolliffe's encephalopathy on the one hand; and Scott's central neuritis, pellagra and beriberi on the other. There is agreement in the literature now, that all depend on lack of one or more factors of the B complex. There are no sharp boundaries between them in many respects. I do not wish to confuse clearly cut cases of beriberi and pellagra, but mixed forms of deficiencies of many factors of the B complex are common in nature. I cannot find in the literature nor have I seen a case of cardiac disorder caused by pellagra, nor a case of stomatitis or dermatitis by beriberi. As soon as we touch the nervous system, however, the two causes may easily overlap. On the whole we may state that beriberi is more liable to affect the peripheral nerves, and pellagra (and central neuritis, as observed by Scott [107]) more the central nervous system. However, the ophthalmoplegia in Wernicke's syndrome is by Jolliffe et al. [52] regarded to be a B_1 symptom; Alexander et al. observed experimental haemorrhagic polioencephalitis (Wernicke) in pigeons deprived of thiamin whereas other vitamins were fed in large quantities [1]. On the other hand in all post mortems in pellagrins degeneration of the peripheral nerves is noted, be it to a lesser degree than in the central nervous system. Certainly the former may also be dependent on concomitant lack of B_1.

19. Neuropathia nervi optici (Schwartz)

Ophthalmic examination was performed by Schwartz in the 160 group. In addition Schwartz observed ± 500 more cases and probably will publish his findings shortly.

In 50 of 160 cases *retrobulbar neuritis* was found, or *neuropathia nervi optici*, the name suggested by Schwartz. In several papers read in the P.O.W. camp at Bandoeng he reported his findings (1942—1943)[106]. In most of the cases there were no abnormalities to be seen in the fundi, however, not infrequently pallor of the optic discs was observed. Of the 50 cases with oto-neurological disturbances 9 had hyperaemic discs, 2 in one and 7 in both eyes. The visual acuity might vary considerably in these 50 patients, from 1/6 to 6/6. In one patient vision might vary in acuity as well. Normal vision was not uncommon, neuritic changes only manifesting themselves by scotomata. For other ocular disturbances the reader may be referred to the preceding sections.

From a personal communication by Mohr[78] in 1944 at Batavia and from Moorrees[83] in some lectures in Pakan Baroe camp, I learned more of the initial stages, observed in Sourabaia in 1942. Many *hyperaemic oedematous fundi* were observed there, occasionally with small haemorrhages. *Scotomata* were common and varying in form, size and existence. Later *pale discs* preponderated. Mohr †, all whose data and drawings of fundi, covering a period of 2 years, were burnt by a Japanese camp commander, told me he had reasons to assume a suprachiasmal cause in several cases. A short time later he was drowned.

Comment

In the "Nederlandsch Tijdschrift voor Geneeskunde" publications on amblyopia in allied prisoners during this last war have appeared from Dekking[28], Soewarno[115] and Van Manen[73]. Métivier, Landor and Pallister, Moore, Stannus and Wilkinson and King reported the same in deficiencies. Not to repeat the same story too often we will state merely that partly nicotinic acid, partly riboflavin and partly both are found to be effective[11, 74]. Refer also to the comment on vestibular cold stimulation in this work.

20. General examination

Smitskamp and Jenner were so kind as to examine my patients. Smitskamp in addition made a microscopic study of the capillar vessels under the nails of fingers and toes in relation to burning hands and feet. His findings will be published shortly.

Of this group of 160 patients in 30 cases the capillaries of fingers and toes were too narrow, once too wide and tortuous, and once tortuous.

On the whole the blood pressure perhaps was a little low, in 10 cases 110 systolic or lower. On the other hand there were eleven cases with a systolic pressure of 150 or higher. The sedimentation test showed little abnormality, nor did the cell count and differential count. In 6 cases a moderate leucopenia (3—5000) was found. A moderate anaemia with normal or slightly reduced colour index was occasionally observed. Some patients had oedema of both legs, or only pretibial. In Pakan Baroe this number increased enormously: beriberi, famine oedema, or both.

In the last months at Bandoeng it was possible to examine the gastric juice; in about 30 patients so tested there was consistently a marked hypo- or achlorhydria.

Comment

There is little characteristic in the findings in Bandoeng, but for the hypochlorhydria. This is a constant finding in pellagra [20, 74, 11, 33] etc. The underlying pathology of this symptom is a gastritis which can be demonstrated gastroscopically in many pellagrins (Justin-Besançon). He regards this gastritis with severe hyperaemia and oedema of the mucous membrane as "perhaps the most constant of all manifestations of pellagra"[53]. L. Simons found this gastritis frequently in our post mortems, in these end stages

there are often additional areas of atrophy, being the result of many exacerbations and remissions.

With lack of hydrochloric acid in the gastric juice vitamin B_1 taken orally is largely destroyed [11]. This may be one of the causes of allied B_1 deficiency in pellagra.

Reports on the blood pressure in pellagra are rather vague in the literature; on the whole there is a tendency to regard a low blood pressure as fitting in the disease picture. However Monteiro et al. note a high blood pressure in many cases of pellagra in Northern Portugal [79]; Harrison notes it in malnutrition in P.O.W.s at Hongkong [49].

Interesting is in this respect that Van Schoonhoven van Beurden, finding nicotinic acid curative in infantile acrodynia (Swift-Feer), considers the high blood pressure in acrodynia as one of the differences from pellagra [105].

21. Skin

Hurwitz†, Van der Meer and R. Simons [112] observed in 1942 at Bandoeng many cases of *hyperkeratosis pilaris* on the surfaces of *elbows* and *knees* and *seborrhoic eczema* of the *nose* and *nasolabial folds*.

The *"scrotal rash"* was frequently observed, a typical affection. The front of the scrotum is red, rather sharply limited, very sharp towards the middle line, the raphe scroti is free. There may be scaling and dryness, there is often itching. At first the condition was attributed to bad soap, or to the absence of soap; the soldiers called it Bandoeng-, Sourabaia- or Java-balls. I saw many of these patients and the affection was always limited to the front of the scrotum, in two strictly separated red patches. To see them the patient must be told to lift his penis. Not unfrequently it causes no complaint and the patient is quite astonished that the physician knows of its existence. It was frequently accompanied by soreness of the mouth and pharynx, etc. Of our 160 cases 37 showed or reported the scrotal lesion.

Only two of the 160 showed *typical pellagrous dermatitis*, these were cases from Sourabaia where they suffered much worse conditions than we at that time. In Sourabaia

Krijnen demonstrated several cases of dermal pellagra as early as September 1942. Altogether approximately 15 cases of typical dermatitis came to our camp from Sourabaia in April '43. I believe in Bandoeng not a single case developed typical dermal lesions, our conditions at that time appeared to be not bad enough to bring this symptom out.

Comment

In July 1943 I read a paper in the Bandoeng camp, in which I suggested pellagra to be the cause of the oto-neurological syndrome described in this thesis [96]. This was not believed by many because of the absence of typical pellagrous dermatitis.

Later, in Pakan Baroe, many nystagmus cases developed typical dermatitis, which is too well known to describe it here, not infrequently with blisters. Even there the tendency was frequently observed to rule pellagra out in the absence of dermal lesions. Many people died from uncontrollable diarrhea, with sore mouth, pharyngitis and oesophagitis, with retrobulbar neuritis and oto-neurological disturbances in different combinations, without the obvious diagnosis pellagra, because there were no dermal signs. Paralytic patients over there now and again were put in the sun on stretchers. They liked this very much, for a short time. We arranged this for some of the patients with the abovementioned picture and nearly all immediately developed dermatitis. It was stopped very soon though, because they withered like a flower, the sun having a deleterious influence not only on the skin, but also on the general condition and on the diarrhea (L. Simons). This phenomenon, among others noted by Castellani, Chalmers [20], Ruffin and Smith [74] was not known to me at that time. Furthermore with great difficulty we arranged for post mortem examinations (fig. 4, L. Simons) and found affection of the whole digestive tract and not only of the large bowel and lower part of the ileum, as would be expected in cases of chronic dysentery.

Moore, Spies and Cooper examined specimens of skin from pellagrins, taken from affected as well as from

unaffected parts. In both they found atrophy, dyskeratosis and inflammation; and much more marked vasodilatation and oedema in the affected parts [82]. Unfortunately I did not find observations in the skin of pellagrins without dermatitis in the literature. However, it will be clear, that the skin has pellagra, whether affected by the typical dermatitis, or not. The same is true of its owner. Goldberger states that the dermal affection may appear late; that in the case of typical dermatitis the diagnosis is made by the layman in the endemic area [44]. In the absence of macroscopically visible dermatitis difficulties in diagnosis arise, even for the physician. Castellani and Chalmers as early as 1919 write: "If no cutaneous symptoms are visible, it is justifiable to place the patients in strong sunlight in order to see whether dermatitis will appear" [20]. However, beware of this diagnostic method, for the abovementioned reason. Often patients know this general effect of sunlight by bitter experience, and shun it. Often photophobia enforces this tendency. Paralysis in the end stages makes a stay in the sun impossible. In many countries sunshine is rare, and it is in these countries that cutaneous symptoms often will be awaited in vain. All the enumerated facts will render it more or less difficult for the pellagrous skin to react with the typical dermatitis and in this way to show frankly the bad condition of the patient.

On the whole I think that pellagra sine pellis agra is now a well recognised clinical picture [11, 33, 20, 74, 13, 142, 39, 32, 51, 70, 82, 119], etc.

One more remark on the typical skin affections: they are described as symmetrical, and mostly are so. Bean, Vilter and Spies, however, reported asymmetry in cases where the blood flow to the affected part was impeded [7].

The scrotal dermatitis is a much earlier symptom, appearing at the same time as vertigo, oral lesions, burning hands and feet, etc. Goldberger and Wheeler in their Rankin Prison Farm experiment saw it develop in a high percentage and were led to believe that the earliest sign of dermal affection was the scrotitis [42]. It was reported by several others also and by some held to be a riboflavin deficiency [11, 33]. However, Van der Meer (Bandoeng) saw the lesion vanish on

administration of diaethyl nicotinamide. By several authors the lesion is described to extend on the inner surfaces of the thighs and on the perineum [11, 101], we never saw this. I know from my own experience the scrotal dermatitis is often overlooked, by the patient as by the physician. When present, they are in the form described above, typical of a B_2 complex deficiency.

Summary

Neurological findings were little marked in Bandoeng, frequent and full-blown in Pakan Baroe. Premortal delirium and coma were not infrequently observed. One nystagmus case died with a picture of Wernicke's encephalopathy (post mortem); one with Korsakoff's syndrome. Some cases resembling Jolliffe's nicotinic acid deficiency encephalopathy [51] were observed.

In the general examination at Bandoeng probably the most consistent symptom was a- or hypochlorhydria. In 31 cases out of 160 abnormalities in capillary width of the fingers and toes were observed.

Ophthalmically, retrobulbar neuritis occurred in 50 out of 160 cases. Pellagrous dermatitis was rare at Bandoeng (2 of 160), being much more frequent at Pakan Baroe. Scrotal dermatitis was frequently observed in the earlier stages and is considered to be an early typical B_2 complex deficiency symptom.

CHAPTER III. STATISTICS, CASE REPORTS

A table on the 160 Bandoeng patients follows. At some places the writing became illegible from moisture, in other cases some points in the history or examination were not recorded; hence the occasional question marks.

Explanation on table

Column 2, Nationality: *D* = *D*utch.
M = *M*enadonese, from Menado, on the island of Celebes, Dutch East Indies.
E = *E*urasian.
B = *B*ritish.
T = *T*urk.
C = *C*hinese.
A = *A*ustralian.
Am = *Am*bonese, from the island of Ambon, Spice Islands.
WI = Eurasian from the Dutch *W*est *I*ndies.

Column 4: Weight in kilograms; the 2nd column is the lowest weight during captivity up to the moment of examination, the 3rd is the last known weight before the examination.

Column 20: *scd* = slight *c*onduction *d*eafness.
pdl = *p*erception *d*eafness *l*eft ear.
md = *m*ixed *d*eafness (in both ears).
underlined = caused by deficiency.

Column 21: *la* = *la*crimation.
bu = *bu*rning and (or) itching of the conjunctivae.
+ = blurred vision.
p = *p*hotophobia.

Column 22: *h* = *h*yperaemic optic disc(s).
n (l) = retrobulbar *n*euritis (*l*eft side).
nb = *n*ight *b*lind.

Column 23: *sw* = *sw*aying of considerable degree.
+ l = positive to the *l*eft, independent of head position.
+ b (r) = positive *b*ackwards (and to the *r*ight, obliquely), independent of head position.
+ o = positive to the *o*cciput, (dependent upon head position).
+ re = positive to *r*ight *e*ar, (dependent on head position).

Column 24: *+ l* = deviation to the *l*eft.
sw = *sw*erving to both sides.
a = *a*taxic.
f (l) = *f*alls (to the *l*eft).

Column 25: *+l* = both arms to the *l*eft.
l+r = *l*eft arm to the *r*ight.
+ow = both arms *o*ut*w*ard.
sd = past pointing in several *d*irections.
} Exceeding 5 cm.
+dw = both arms *d*own*w*ard, exceeding 10 cm.

Column 26: One figure is Atkinson's quotient, for both ears.
2—4 = right ear 2, left ear 4.
— = sudden falling or another untoward reaction, so that no observations were made. Or, for one ear —, means that the second ear was not tested because of unpleasant reactions on the first one.

Column 27: *r+* = from Atkinson's stimulation of *r*ight ear no rotatory nystagmus.
+ = the same for both ears.

Column 28: *rnp* = stimulation *r*ight ear gives *n*o past *p*ointing.
rpl = stimulation *r*ight ear gives past *p*ointing to the *l*eft.
bcl = stimulation of *b*oth ears gives outward deviation of the *c*ontra*l*ateral arm.
spa = *s*pontaneous past *p*ointing *a*bolished by stimulation.
rRb = stimulation of *r* ear gives *R*omberg *b*ackwards.

Column 29: *+* = nystagmus to one or both sides.
++ = nystagmus very marked, though still 1st degree.

Column 33: *a* = *a*taxia of convergence movements.

Column 35: *ra* = *r*eflexes *a*ggravated (markedly or exceedingly).
rl = *r*eflexes *l*ow.
rd = *r*eflexes *d*ifferent right and left.
ds = disturbance *d*eep sensibility.
ss = disturbance *s*uperficial *s*ensibility.
a = *a*taxia.

Column 36: *nf* = much *n*eutral *f*at in the faeces.
95—55 = blood pressure systolic and diastolic respectively.
S 79 = haemoglobin Sahli 79 % (corrected).
nc (w) (t) = *n*arrow *c*apillaries (*w*ide) (*t*ortuous) of fingers and (or) toes.
*ST*19 = *s*edimentation *t*est 19 mm. in the first hour.
l = *l*eucopenia (3—5000).
lc = *l*eucocytosis.
o = *o*edema.

Column 37: Nylen II = positional nystagmus type II Nylen.

TABLE SHOWING 160 BANDOENG PATIENTS

1. Number	2. Nationality	3. Age	4. Weight			5. Perlèche	6. Cheilosis	7. Stomatitis	8. Pharyngitis	9. Scrotal dermat.	10. Burning h. & f.	11. Diarrhea	Vertigo			15. Nausea, vomiting	16. Sweating	17. Headache	18. Tinnitus	Hearing loss	Eyes		23. Romberg test
			Before war	Lowest	Now								12. Rotatory	13. „Black out"	14. Other forms					19. Subjective	20. Objective	21. Subjective	22. Objective	
1	D	48	?	?	?	?	?	?	?	?	?	?	+	—	—	+	+	—	—	?	scd	?	h	—
2	D	36	?	?	?	—	—	—	—	—	—	—	+	—	—	—	?	?	+	+	spd	—	—	—
3	D	39	63	53	62	—	—	—	—	+	+	—	+	—	—	+	—	+	—	—	pd	—	—	—
4	D	41	91	78	80	+	—	—	—	—	—	—	—	—	—	+	—	—	—	—	md	—	—	sw
5	D	26	?	?	?	—	—	—	—	—	—	—	+	—	—	—	+	—	—	+	spd	la	—	—
6	D	30	?	?	?	?	?	?	?	?	+	—	+	—	—	—	+	+	—	—	spd	—	—	—
7	D	38	92	72	76	—	—	—	—	—	—	—	+	—	—	+	+	—	+	+	pdl	—	—	—
8	D	47	80	63	66	—	—	—	—	—	+	—	—	—	—	—	—	—	—	—	spd	p	—	sw
9	D	35	66	54	?	—	—	—	—	+	+	—	+	—	—	—	—	—	+	+	md	—	n, h	—
10	D	46	?	?	?	—	—	—	—	—	—	—	+	—	—	+	—	—	+	—	—	—	—	—
11	D	26	?	?	?	—	—	—	—	—	—	—	+	—	—	+	+	—	+	+	pdl	p	—	sw
12	D	48	83	68	71	—	—	—	—	—	+	+	—	+	—	—	—	+	—	—	spd	+	n	—
13	D	38	72	61	64	—	—	+	—	+	+	+	—	—	—	+	—	—	—	—	spd	bu	—	—
14	D	46	?	?	?	—	—	—	—	—	—	?	—	—	—	+	+	—	—	—	pd	—	n, h	+ l
15	D	51	80	63	71	—	—	—	—	—	+	—	—	—	+	—	+	—	—	—	pd	+	n, nb	+ r
16	M	24	?	?	?	+	+	+	+	—	+	?	—	—	—	—	—	—	—	—	—	—	h	—
17	D	47	95	68	71	—	—	—	—	—	+	—	—	—	—	—	—	—	—	+	pd	la	—	?
18	D	29	?	?	?	—	—	—	—	+	+	?	+	—	—	+	+	+	—	—	spd	—	—	+ b
19	E	50	65	53	53	—	—	—	—	—	+	—	—	—	—	—	—	—	+	?	pd	+ p	n	+ o
20	D	33	?	?	?	—	—	—	—	—	+	+	+	—	—	—	—	+	—	—	spd	—	—	—

24. Walking test	25. Pointing test	26. Atkinson test	27. Eagleton	28. Perversities on Atkinson test	29. Nystagmus	30. Nystagmoid	31. Praenystagmus	Weakness of		34. Anisocoria	Examination		37. Further particulars	38. Number
								32. Lateral gaze	33. Convergence		35. Neurological	36. General		
—	—	15	—	—	+	—	—	—	—	—	—	—		1
—	—	14	—	—	+	—	—	+	+	—	—	—		2
+ l	—	10	—	rnp	—	+	+	+	—	—	ra	nf		3
+ l	—	6 — —	—	—	+ +	—	—	+	+	—	—	—		4
+ l	+ l	7	—	rpl	+	—	—	+	—	—	rd	95—55		5
—	—	30	—	—	+ +	—	—	—	+	—	—	—	Osc. N. in uw. gaze, mydriasis, later dermal pellagra.	6
—	—	4—$\frac{1}{3}$	—	—	—	—	+	—	—	—	—	—		7
—	1 + 1	14	—	—	+	—	—	+	—	—	ra	—		8
—	—	12	—	lcl	+	+	+	+	—	—	—	—		9
—	—	6	—	—	+	—	—	—	—	+	—	—		10
sw	—	10—2	—	—	+	—	—	+	?	—	—	—		11
—	—	3½	—	—	+ +	—	—	+	—	—	ra	nf		12
—	—	6½	—	—	+	—	+	+	—	—	—	—		13
+ r	+ l	12—14	—	rnp	—	+	—	+ +	+ +	—	wtl	—		14
—	—	12	—	—	—	+	+	+	?	—	—	162—75 S 79		15
—	—	10	—	—	+	—	—	+	?	—	ra	nc		16
sw	—	12	—	—	+ +	+	—	—	—	—	ra	—		17
+ r	—	10	—	—	+	+	—	+	—	+	ds, ss	105—80 nc	Nylen II	18
sw	sd	11—9	—	—	+	—	—	—	—	—	ss, a	155—110 nc		19
?	?	10	—	rcl	+	—	—	—	+	—	ra	nc		20

1. Number	2. Nationality	3. Age	4. Weight: Before war	4. Weight: Lowest	4. Weight: Now	5. Perlèche	6. Cheilosis	7. Stomatitis	8. Pharyngitis	9. Scrotal dermat.	10. Burning h. & f.	11. Diarrhea	Vertigo: 12. Rotatory	Vertigo: 13. „Black out"	Vertigo: 14. Other forms	15. Nausea, vomiting	16. Sweating	17. Headache	18. Tinnitus	Hearing loss: 19. Subjective	Hearing loss: 20. Objective	Eyes: 21. Subjective	Eyes: 22. Objective	23. Romberg test	24. Walking test	25. Pointing test	26. Atkinson test	27. Eagleton	28. Perversities on Atkinson test	29. Nystagmus	30. Nystagmoid	31. Praenystagmus	Weakness of: 32. Lateral gaze	Weakness of: 33. Convergence	34. Anisocoria	Examination: 35. Neurological	Examination: 36. General	37. Further particulars	38. Number
21	D	47	73	59	62	—	—	—	—	—	+	—	+	—	—	—	—	—	+	+	spd	—	—	+1	sw	1+1	12—11	—	bnp	—	—	+	+	+	—	ss, ra	nc	† Korsakoff	21
22	D	32	68	55	57	?	?	?	?	?	+	?	—	—	—	—	+	+	—	+	—	—	—	—	—	—	7—8	—	bcl lnp	++	—	—	—	a	+	—	165—90		22
23	D	35	84	63	66	—	—	—	—	—	+	+	+	—	—	—	—	—	—	—	—	p, la	h	—	—	—	6	—	—	+	+	—	—	—	—	ra	nc		23
24	D	29	63	?	63	—	—	—	—	—	—	—	+	—	—	+	+	—	—	—	spd	—	—	—	—	—	14	—	—	—	+	—	+	—	—	—	170—95		24
25	D	28	76	59	69	—	—	—	—	+	+	+	—	+	—	+	+	+	+	—	spd	—	—	—	—	sd	13	—	bcl	++	+	+	—	—	—	a, ra	nc		25
26	D	44	106	74	77	—	—	—	—	—	+	—	+	—	—	—	—	—	—	—	pd	p	—	sw	—	—	9	—	—	+	—	—	—	—	+	—	nc		26
27	D	33	72	65	69	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	+	n	—	—	—	6—5	—	—	+	—	+	+	—	+	rd	nc	hor. osc. N. in uw. gaze	27
28	D	47	115	85	95	—	—	—	—	—	+	—	—	—	—	—	+	+	—	—	spd	+	—	sw	+ r	+ dw	10	+	—	—	—	—	+	—	—	ss	—		28
29	D	42	85	71	73	—	—	—	—	—	+	+	—	+	—	—	—	—	—	—	spd	+	n	—	—	—	10	—	—	+	—	+	—	—	—	—	nc		29
30	D	44	76	62	?	+	—	+	—	+	+	+	—	—	—	—	—	+	—	—	—	+	n	sw	f	sd	—	—	—	—	+	—	+	a	+	ss	—	Pick's visions	30
31	B	21	75	?	?	?	?	?	?	?	+	?	—	+	—	—	—	—	—	—	—	+	n	—	—	—	9	—	—	++	—	—	+	?	—	—	—		31
32	D	?	82	68	72	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	spd	—	—	—	—	—	6	—	—	+	—	+	—	—	+	—	?		32
33	D	37	65	42	60	—	—	—	—	—	—	+	—	?	—	+	—	+	—	—	—	bu	n	sw	—	—	6	—	—	—	—	+	—	—	—	ra	—		33
34	D	47	113	80	80	—	—	—	—	—	+	+	+	—	—	—	—	—	+	—	spd	—	n	sw	a	—	4—10	—	—	—	+	—	++	++	—	ds, a	nc		34
35	D	46	87	69	71	—	—	—	—	—	—	—	—	—	—	+	—	—	+	—	pd	+	—	sw	sw	sd	14	—	lcl spa	+	+	—	+	+	—	ra	—		35
36	D	25	72	75	?	—	—	—	—	—	—	—	—	—	—	+	—	—	—	—	spdl	—	—	sw	sw	—	12	—	—	+	—	—	+	++	—	ss	150—88 nc		36
37	B	24	57	50	61	—	—	—	—	—	—	?	—	+	—	—	—	—	+	—	—	—	—	—	—	—	7	—	—	+	—	—	+	—	—	?	?		37
38	D	27	80	67	69	—	—	—	—	—	—	—	—	—	—	—	+	—	+	—	—	p	n	—	+ r	—	18—15	—	—	+	—	—	—	—	—	a	?	Nylen I	38
39	D	39	67	55	57	—	—	—	—	+	—	—	—	—	—	+	—	—	—	+	spd	—	?	—	—	—	10	—	—	+	—	—	—	—	+	—	?		39
40	D	47	92	68	80	—	—	+	—	—	+	—	—	—	—	—	—	—	—	—	pd	+	n	+1	+1	lsd	13	+	—	—	+	—	++	++	—	a	nc		40
41	D	48	64	?	66	—	—	—	—	—	—	—	+	—	—	—	+	+	—	—	pd	—	—	—	—	sd	6	—	—	—	—	+	+	+	—	—	ST 19		41
42	D	35	?	?	?	?	?	?	—	?	+	?	+	—	—	+	+	+	—	—	—	?	—	—	—	—	16	—	—	—	—	+	+	+	—	a	110—80		42
43	D	36	115	87	90	?	?	?	—	?	?	?	—	+	—	—	+	—	+	±	—	pd	?	—	+1	1+1	11	—	—	—	—	+	++	++, a	—	—	?		43

1. Number	2. Nationality	3. Age	4. Weight: Before war	4. Weight: Lowest	4. Weight: Now	5. Perlèche	6. Cheilosis	7. Stomatitis	8. Pharyngitis	9. Scrotal dermat.	10. Burning h. & f.	11. Diarrhea	Vertigo: 12. Rotatory	Vertigo: 13. „Black out"	Vertigo: 14. Other forms	15. Nausea, vomiting	16. Sweating	17. Headache	18. Tinnitus	Hearing loss: 19. Subjective	Hearing loss: 20. Objective	Eyes: 21. Subjective	Eyes: 22. Objective	23. Romberg test	24. Walking test	25. Pointing test	26. Atkinson test	27. Eagleton	28. Perversities on Atkinson test	29. Nystagmus	30. Nystagmoid	31. Praenystagmus	Weakness of: 32. Lateral gaze	Weakness of: 33. Convergence	34. Anisocoria	Examination: 35. Neurological	Examination: 36. General	37. Further particulars	38. Number
44	T	28	66	60	65	+	+	+	+	+	+	?	—	—	—	—	—	—	—	—	—	scd	+ p	—	—	—	11	—	bcl	+	—	+	+	+	—	—	—		44
45	D	30	76	62	?	—	—	—	—	+	+	+	·	+	—	—	—	—	—	—	—	spd	p	n	—	—	12	—	—	+ +	—	—	+	+	—	—	S 81		45
46	B	26	72	54	64	+	—	—	—	+	+	+	—	+	—	—	—	—	—	—	—	—	—	—	—	—	9	—	—	+ +	—	—	+	+ +	+	ss	—		46
47	B	28	58	57	62	—	—	—	—	+	+	+	—	—	—	—	+	—	+	—	—	—	+	—	+ 1	1 + 1	9	—	—	—	+	+	+	—	—	ra	—		47
48	D	45	65	54	56	+	—	—	—	+	+	+	—	—	—	—	+	—	—	—	—	md	—	—	+ 1	—	12	—	—	+	—	+	+	—	—	—	—		48
49	E	47	68	50	52	—	—	—	—	—	+	—	+	—	—	—	—	—	—	—	±	pd	—	n	sw	sd	12	1 +	—	—	+	—	—	—	—	a, ss	—		49
50	D	41	78	78	78	+	—	—	—	—	+	+	—	+	—	—	—	—	—	—	+	spdl	—	—	sw	+ ow	6	—	—	+	—	—	+	+	—	a, ss	l		50
51	D	30	76	70	86	—	—	—	—	+	+	—	—	+	—	—	—	—	+	—	—	pd	p	—	—	sd	10	—	spa	—	+	+	+	+	—	a	—		51
52	B	35	?	?	?	—	—	—	—	—	—	—	—	—	—	—	—	—	+	—	—	spd	p	—	—	—	9	—	—	+	—	+	—	+	—	—	—		52
53	D	33	75	75	75	—	—	—	—	—	+	—	—	+	—	—	—	—	—	—	—	spd	—	—	—	—	8	—	lcl	+ +	+	—	+	—	—	—	—		53
54	D	27	70	70	70	—	—	—	—	—	—	+	+	—	—	—	—	—	—	—	—	—	p	—	sw	—	6—3	—	—	+ +	—	—	—	—	—	a	100—90 nc		54
55	D	47	65	63	64	—	—	—	—	—	—	—	—	—	—	+	—	—	—	—	—	pd	—	—	—	—	8	—	—	+	+	—	+	—	+	—	—		55
56	D	25	85	90	83	—	—	—	—	—	+	+	—	—	—	+	+	+	—	±	—	pd	la	—	—	sw	11	r +	rcl	+	+	—	+	+	—	a	—		56
57	E	61	76	55	61	—	—	—	—	—	+	—	+	—	—	—	—	—	—	+	+	pd	+	n	sw	sd	—	—	—	—	—	+	+	+	—	ra	nc		57
58	B	40	78	62	64	—	—	—	—	—	+	—	—	—	—	+	—	—	—	±	—	—	+	—	+ r	1 + 1	20	—	lcl	—	—	+	+	+	—	—	—		58
59	D	58	85	71	72	—	—	—	—	—	+	—	—	+	—	—	—	—	—	—	—	cd	+	n	—	—	10	—	—	—	+	—	—	—	—	a	S 87, nc		59
60	B	27	71	62	74	—	—	—	—	—	—	+	—	+	—	—	—	—	—	—	—	cd	bu	—	—	1 + 1	12	—	—	—	+	—	—	—	+	—	?		60
61	D	27	65	59	62	—	—	—	—	—	—	+	—	+	—	—	+	+	—	—	+	—	+	—	—	—	9	—	—	+ +	—	—	+	—	—	—	—		61
62	E	43	?	?	?	—	—	—	—	—	+	—	+	—	—	—	+	+	—	—	—	cd	+	n	—	—	9	1 +	—	+	—	—	—	—	—	ss	ST 38		62
63	B	34	89	77	80	—	—	—	—	+	+	+	+	—	—	—	—	+	+	+	—	cd	—	h	sw	—	12	—	—	+	—	—	—	—	—	—	S 88		63
64	B	34	72	67	68	—	—	—	—	—	+	+	—	—	—	—	+	—	+	—	+	cd	—	—	+ r	—	6	—	lcl	—	—	+	+	+	—	—	155—95 S 81	Hertw.-Mag.	64
65	C	22	?	?	?	+	—	+	—	—	—	—	—	—	—	+	—	—	—	±	±	spd	—	—	—	—	6	+	—	—	—	—	+	+ +	—	—	?	hor. osc. N. ↓	65
66	B	32	87	57	58	+	+	—	+	—	—	—	—	—	—	—	+	—	+	—	—	—	+	—	sw	—	12	—	—	—	+	—	—	+	+	—	—	l		66

1. Number	2. Nationality	3. Age	4. Weight			5. Perlèche	6. Cheilosis	7. Stomatitis	8. Pharyngitis	9. Scrotal dermat.	10. Burning h. & f.	11. Diarrhea	Vertigo			15. Nausea, vomiting	16. Sweating	17. Headache	18. Tinnitus	Hearing loss		Eyes		23. Romberg test
			Before war	Lowest	Now								12. Rotatory	13. „Black out"	14. Other forms					19. Subjective	20. Objective	21. Subjective	22. Objective	
67	B	29	72	60	64	+	+	+	—	+	+	+	+	—	—	—	—	+	—	—	spd	+ p	n	—
68	B	33	?	?	70	—	—	—	—	—	+	—	—	—	—	—	—	+	—	—	scd	—	—	—
69	D	44	85	76	76	—	—	—	—	—	+	+	+	—	—	+	—	—	—	+	pd	—	—	+ bl
70	D	35	73	75	75	—	—	—	—	—	—	+	—	—	+	—	—	—	—	—	pd	—	—	—
71	E	49	72	58	65	—	—	—	—	—	+	—	—	—	+	—	—	—	+	+	pd	—	—	sw
72	D	31	80	69	83	—	—	—	—	—	—	—	—	+	—	—	—	—	—	—	—	p, bu	—	sw
73	D	37	85	77	77	—	—	—	—	—	+	+	—	—	+	+	—	—	—	—	scd	—	—	—
74	D	40	92	65	71	—	—	—	—	+	+	—	—	—	+	—	—	—	—	—	cd	—	—	—
75	E	36	?	51	57	+	—	—	—	+	+	+	—	—	+	—	—	—	+	—	md	p	h	—
76	D	35	93	77	79	—	—	—	—	—	+	—	—	—	—	—	—	+	—	—	spd	—	n	—
77	D	48	83	60	60	—	—	—	—	—	+	+	—	+	—	+	+	+	—	—	md	+	—	sw
78	D	27	78	68	78	—	—	—	—	+	—	+	—	—	+	+	—	+	—	—	spd	bu	—	—
79	B	27	78	60	69	+	+	+	—	+	+	+	—	+	—	—	—	—	—	—	cd	—	n	—
80	B	28	68	48	64	+	—	—	—	—	+	+	—	—	+	—	+	—	+	—	pd	p	—	sw
81	E	37	71	58	62	—	—	—	—	—	+	+	—	—	—	+	+	+	+	—	—	—	—	—
82	D	49	86	69	71	+	—	—	—	+	+	+	—	—	+	+	—	+	—	—	spd	+	n	sw
83	E	20	?	?	63	—	—	—	—	—	—	—	+	—	—	+	+	+	+	—	pd	—	—	sw
84	D	48	68	55	60	—	—	—	—	—	—	—	—	+	—	—	—	+	+	—	md	—	—	—
85	D	48	86	72	72	—	—	—	—	—	—	+	—	—	+	?	?	?	+	+	pdl	la	—	—
86	A	40	83	76	77	—	—	—	—	—	—	—	—	—	—	+	+	+	—	—	spd	+	—	+ re
87	D	43	78	62	63	+	—	—	—	+	+	+	—	—	—	+	+	+	+	+	md	—	nl	sw
88	D	47	82	70	71	—	—	—	—	—	+	+	—	—	+	+	—	+	+	—	md	+	n	—
89	E	46	66	59	59	—	—	—	—	—	—	—	—	—	—	+	—	+	+ l	—	pd	+ bu	—	sw

24. Walking test	25. Pointing test	26. Atkinson test	27. Eagleton	28. Perversities on Atkinson test	29. Nystagmus	30. Nystagmoid	31. Praenystagmus	Weakness of		34. Anisocoria	Examination		37. Further particulars	38. Number
								32. Lateral gaze	33. Convergence		35. Neurological	36. General		
+ l	—	14—2	—	—	+	—	—	+	+	—	ds	—		67
—	—	8	—	—	+	—	—	—	—	—	—	—		68
+ l	sd	10	—	—	—	—	+	+	+	—	a, ra	?		69
—	+ dw	9	—	—	+ +	—	—	—	+	—	—	nc		70
—	—	11	—	lcl	+	+	+	+	+ +	—	ss	160—75 lc		71
sw	—	2½	—	rcl	+	—	—	+ +	a	—	sds, ra	105—60		72
fr	+ ow	11	—	?	—	—	—	+	—	—	a, ra	—		73
—	+ l	16	—	lcl	—	+	+	+	—	—	—	ST 20		74
a, f	+ ow	—	?	?	+	+	—	+	+	+	ra	—		75
—	—	4—5	l +	—	+	—	—	—	—	—	—	nc		76
—	l + l	20	—	bcl	+	—	—	+	+	—	ss, a	—		77
—	—	8	—	—	+	+	—	+	+	+	—	—		78
—	—	6	—	—	+	—	—	—	—	—	—	—		79
a	—	9	—	—	+	—	—	—	+	—	—	nc		80
—	—	6	—	—	—	+	—	+	+	—	—	nc		81
+ r	sd	14	—	—	+	+	+	—	+	—	—	tc, S 82		82
+ l	—	6½—4	—	—	+	—	—	—	—	—	ra	—		83
—	+ ow	8	—	—	+ +	—	+	+	+	—	—	—		84
a	r + dw	5	—	—	+	—	+	+	+	—	—	—		85
+ r	l + l	11 — —	—	—	—	+	—	—	+	—	—	nc		86
+ r	sd	10	—	—	+	+	—	+	+	—	—	—		87
+ l	—	9	—	—	+	—	—	+	—	+	ss, a	S 82		88
a	sd	16—10	r +	—	—	+	—	+	+	+	ds	—		89

1. Number	2. Nationality	3. Age	4. Weight			5. Perlèche	6. Cheilosis	7. Stomatitis	8. Pharyngitis	9. Scrotal dermat.	10. Burning h. & f.	11. Diarrhea	Vertigo			15. Nausea, vomiting	16. Sweating	17. Headache	18. Tinnitus	Hearing loss		Eyes		23. Romberg test
			Before war	Lowest	Now								12. Rotatory	13. „Black out"	14. Other forms					19. Subjective	20. Objective	21. Subjective	22. Objective	
90	D	46	78	56	68	—	—	—	—	—	—	+	—	—	—	—	—	+	—	—	—	p	—	—
91	B	37	63	48	55	+	+	+	—	+	+	+	+	—	—	+	+	+	—	—	pd	+	—	+ rl
92	E	34	68	59	59	—	—	—	—	—	+	+	+	—	—	—	+	+	—	+	pd	—	—	—
93	D	48	81	65	73	+	+	—	—	+	+	+	—	—	—	+	+	+	—	—	cd	+	n	+ le
94	D	34	107	67	67	—	—	—	—	—	—	—	—	+	—	?	?	+	±	±	pd	—	—	—
95	D	25	78	71	71	—	—	—	—	—	—	+	—	—	—	—	—	+	—	—	pd	+	n	sw
96	D	39	73	64	66	—	—	—	—	—	+	—	—	—	+	+	—	+	—	—	spd	p, la	—	sw
97	D	44	63	62	?	+	—	—	—	+	+	+	—	—	—	—	—	+	±	—	pd	+	n	—
98	B	32	62	58	62	+	—	—	—	—	+	+	—	—	+	+	—	+	—	—	—	p	—	—
99	D	37	68	45	62	—	—	—	—	—	+	+ +	—	—	—	+	+	+	±	—	—	—	—	sw
100	D	40	72	50	66	—	—	—	—	—	+	+ +	+	—	—	—	—	—	—	—	cdl	+	n	—
101	D	49	92	61	70	—	—	—	—	—	+	—	—	—	+	—	—	—	+	+	spd	—	—	sw
102	E	38	75	69	70	—	—	—	—	—	+	—	—	+	—	—	—	+	—	—	spd	—	—	—
103	D	34	92	76	76	—	—	—	—	—	—	+	+	—	—	—	+	+	—	±	pd	p	—	—
104	D	39	106	74	89	—	—	+	—	—	+	—	—	—	—	+	—	—	—	—	spd	—	—	+ b
105	D	48	83	69	73	—	—	—	—	+	—	+	—	—	—	+	+	—	—	—	spd	p	—	sw
106	Am	43	68	58	59	—	—	—	—	—	+	—	+	—	—	+	—	+	+	—	pd	+	n	—
107	E	21	74	70	?	—	—	—	—	—	—	—	—	—	—	—	+	—	—	—	pd	—	—	sw
108	WI	43	71	55	60	—	—	—	—	—	—	—	—	—	—	+	—	—	+	+	pd	—	—	—
109	D	44	80	58	60	+	+	+	—	—	+	+	—	—	—	—	—	+	+	—	pdl	+	n, h	—

1. Number	24. Walking test	25. Pointing test	26. Atkinson test	27. Eagleton	28. Perversities on Atkinson test	29. Nystagmus	30. Nystagmoid	31. Praenystagmus	Weakness of		34. Anisocoria	Examination		37. Further particulars	38. Number
									32. Lateral gaze	33. Convergence		35. Neurological	36. General		
90	—	—	9	—	—	+	+	—	+	+	—	—	—		90
91	sw	sd	20	—	rnp	—	+	—	+	+	—	a	?		91
92	—	—	10	—	—	—	—	—	—	+ +	—	ra	S 86		92
93	—	sd	12	+	—	—	—	+	+ +	+ +	—	a	ST 18, o, hb 83		93
94	+ r	sd	14	—	rcl	+ +	—	—	—	+	—	—	hb 89		94
95	—	+ r	9—13	—	—	—	+	+	+	+	—	ra	155—95 S 81		95
96	a	a	5	—	—	—	+	+	+	+ a	—	—	180—75		96
97	—	—	21	1 +	—	—	+	—	+	+	—	a, ds	S 82, nc 190—118	pupils irregular	97
98	+ r	—	12 — —	—	—	+	—	—	—	—	—	—	?		98
99	—	—	?	?	?	+	—	—	—	—	—	—	nf		99
100	—	—	6 — ?	—	—	+	—	—	—	+	—	?	nf	perf. L. drum	100
101	a	—	11	+	—	—	+	—	+	+	—	ra	S 87, nc ST 16		101
102	—	—	9	—	—	+	—	—	—	—	—	—	—		102
103	sw	1 + 1	9	—	—	—	+	—	+	—	—	a, rd	—		103
104	a + r	—	7 — —	—	—	+ +	—	—	—	—	—	a, ss	S 89, nc ST 15		104
105	a	1 + 1	22	+	—	—	+	—	+	+ +	—	—	wtc		105
106	sw	—	12	—	—	—	+	+	+	—	+	a	nc	r. pup. irr.	106
107	—	1 + 1	12	—	lcl	—	+	—	—	—	—	—	S 86		107
108	—	—	15—19	1 +	—	—	+	+	+	—	—	—	S 78	dermal pellagra	108
109	+ r	—	14	1 +	—	—	+	—	—	+	+	a	?		109

1. Number	2. Nationality	3. Age	4. Weight			5. Perlèche	6. Cheilosis	7. Stomatitis	8. Pharyngitis	9. Scrotal dermat.	10. Burning h. & f.	11. Diarrhea	Vertigo			15. Nausea, vomiting	16. Sweating	17. Headache	18. Tinnitus	Hearing loss		Eyes		23. Romberg test	24. Walking test	25. Pointing test	26. Atkinson test	27. Eagleton	28. Perversities on Atkinson test	29. Nystagmus	30. Nystagmoid	31. Praenystagmus	Weakness of		34. Anisocoria	Examination		37. Further particulars	38. Number
			Before war	Lowest	Now								12. Rotatory	13. „Black out"	14. Other forms					19. Subjective	20. Objective	21. Subjective	22. Objective										32. Lateral gaze	33. Convergence		35. Neurological	36. General		
110	D	40	59	59	59	—	—	—	—	—	—	+	—	—	+	+	+	—	—	+	scd	—	—	—	—	—	—	rcl	—	+	—	+	+	—	—	nf		110
111	D	48	92	76	83	—	—	+	—	+	+	+	—	—	+	—	—	—	+	+	pd	+	—	—	—	r + l	16	—	—	—	+	+	—	—	a	—	111
112	D	38	74	65	65	—	—	+	—	+	+	+	—	—	+	—	+	+	—	+	pdl	p	—	sw	sw	l + l	12—18	—	—	—	+	—	+	+	+	—	l, nc	112
113	D	47	88	80	87	—	—	—	—	—	+	—	—	—	—	+	—	+	+	+	md	p	—	—	—	—	13	—	—	—	+	—	—	—	+	rl	—	113
114	B	24	68	60	62	—	—	—	—	—	+	+	—	+	—	—	—	—	—	—	pd	la	—	sw	—	r + l	12—16	—	rcl	+	—	—	—	—	—	rl	nc	114
115	D	47	78	61	72	—	—	—	—	—	+	+	—	+	—	—	—	+	+	+	pd	—	—	sw	—	l + l	12—15	l +	—	—	+	—	+	—	—	a	—	115
116	D	46	?	?	?	—	—	—	—	—	+	—	+	—	—	+	+	—	—	—	pdl	—	nb	+ bl	sw	+ ow	16	—	rRb	—	+	+	+	+	+	a, ra	—	116
117	D	30	107	90	89	—	—	—	—	—	+	—	+	—	—	—	—	+	—	—	pd	—	nb	+ b	sw	sd	12—20	—	—	—	+	—	—	—	—	a	l	117
118	E	32	58	53	53	—	—	—	—	—	—	—	—	—	—	—	+	+	—	—	pdl	bu	—	—	sw	sd	14	r +	—	—	+	—	+	+	—	—	—	118
119	C	38	?	?	?	—	—	+	—	—	—	—	—	—	—	—	—	—	—	—	scd	—	—	—	—	—	14	—	—	—	+	—	—	—	—	—	—	119
120	B	21	63	63	61	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	pd	—	—	—	+ l	—	10	—	—	+	+	—	—	+	—	—	—	120
121	D	46	90	72	76	—	—	—	—	—	+	+ +	—	+	—	—	+	—	—	—	pd	+	n	sw	sw	—	18—13	—	—	—	+	—	+	+	—	rl	150—95 S 83	121
122	D	58	70	57	58	—	—	—	—	—	—	—	+	—	—	—	—	—	—	—	md	—	—	—	—	—	9	—	—	+	—	+	+	+	+	—	—	122
123	D	44	68	60	65	—	—	—	—	—	—	+	—	—	—	—	—	—	+	+	md	p	?	—	—	—	?	—	—	—	+	—	—	—	—	ss	?	123
124	D	25	65	75	71	—	—	—	—	—	—	—	—	—	—	+	+	—	—	—	—	p	?	—	—	—	12—9	—	—	+	—	+	—	—	—	—	?	124
125	D	38	70	64	68	—	—	—	—	—	—	—	—	—	—	+	—	+	+	—	pd	—	—	—	—	—	13	—	—	+	+	—	—	—	—	—	l	125
126	D	34	70	51	63	—	—	—	—	—	+	—	—	—	+	—	—	—	—	+	pd	—	—	sw	a	—	14	l +	bcl	—	—	—	—	+	—	a	—	hor. osc. N. ⇄	126
127	D	34	65	58	62	—	—	+	—	—	+	+	—	—	+	—	+	—	+	+	cd	+	n	—	—	—	11—16	—	lcl	+	+	+	—	—	—	ra	—		127
128	B	21	?	?	?	—	—	—	—	—	—	—	—	+	—	—	—	+	—	—	pdl	—	—	—	—	—	9—11	l +	rcl	—	+	—	—	+	—	—	?	dermal pellagra	128
129	D	29	69	69	71	—	—	—	—	—	—	—	—	—	—	+	+	+	—	—	—	—	—	—	—	—	13	—	—	+ +	—	—	—	—	+	—	?		129
130	E	38	72	48	57	+	+	—	—	—	—	—	+	—	—	+	+	+	+ l	+	pdl	—	—	+ re	+ r	l + l	7—3	r +	bnp bnR	+	—	—	—	—	—	—	?		130
131	D	54	87	71	73	+	+	+	+	—	+	—	—	—	+	—	—	—	±	±	pd	+	n	sw	a.	sd	11—14	—	—	+	+	—	+	+	—	rl, ds	S 80		131

1. Number	2. Nationality	3. Age	4. Weight: Before war	4. Weight: Lowest	4. Weight: Now	5. Perlèche	6. Cheilosis	7. Stomatitis	8. Pharyngitis	9. Scrotal dermat.	10. Burning h. & f.	11. Diarrhea	Vertigo: 12. Rotatory	Vertigo: 13. „Black out"	Vertigo: 14. Other form	15. Nausea, vomiting	16. Sweating	17. Headache	18. Tinnitus	Hearing loss: 19. Subjective	Hearing loss: 20. Objective	Eyes: 21. Subjective	Eyes: 22. Objective	23. Romberg test	24. Walking test	25. Pointing test	26. Atkinson test	27. Eagleton	28. Perversities on Atkinson test	29. Nystagmus	30. Nystagmoid	31. Praenystagmus	Weakness of: 32. Lateral gaze	Weakness of: 33. Convergence	34. Anisocoria	Examination: 35. Neurological	Examination: 36. General	37. Further particulars	38. Number
132	D	?	77	60	67	—	—	—	—	+	+	—	—	+	—	—	—	—	—	—	—	+ p	n	—	sw	—	?	?	?	+ +	—	—	—	—	—	ra	110—60 nc	ptosis, mydriasis, Nylen II	132
133	D	?	86	60	78	+	—	+	—	—	+	+	—	+	—	+	+	+	—	—	—	p, bu	nb	—	+ r	—	6? — —	+ ?	rnp	+	—	—	+	+	—	ra	?	Hertw.-Mag.	133
134	D	57	56	42	49	—	—	—	—	—	+	+	—	—	+	—	—	+	+	+	pd	+	n	sw	sw	—	?	?	?	—	+	+	—	+	—	rl	ST 20		134
135	B	25	73	64	66	—	—	—	—	—	—	+	—	—	—	—	—	+	—	—	—	p	—	—	—	—	9—7	—	—	+	—	—	+	—	—	—	?	mydriasis	135
136	E	38	65	54	59	+	—	—	—	—	+	—	—	—	—	—	+	+	—	±	pd	+	n	sw	—	1 + 1	?	?	?	—	+	+	—	—	+	—	?	pup. irr.	136
137	D	?	105	74	80	—	—	—	—	—	+	—	—	—	—	—	+	—	—	—	—	bu	n	sw	sw	sd	?	?	?	+	—	—	—	+	+	ss	108—70		137
138	B	37	66	59	60	—	—	—	—	—	—	—	—	+	—	—	—	—	+	±	pd	—	—	—	—	—	6	—	—	+	—	—	—	+	—	—	?		138
139	D	32	66	63	68	—	—	—	—	+	—	—	—	+	—	+	—	+	—	—	spd	+	n	—	—	—	6	—	—	+	—	+	—	—	—	—	?		139
140	D	28	60	57	60	—	—	—	—	—	+	—	—	—	—	—	—	+	—	—	pd	—	—	+ rl	+ l	sd	6	+	bcl rRb	—	+	—	—	—	—	a	—	Pick's visions	140
141	B	36	?	?	?	—	—	—	—	—	+	+	—	—	—	—	+	+	+	+	cd	—	—	—	+ l	—	?	?	?	—	—	+	—	a	—	ra	?	pup. irr.	141
142	B	26	?	?	?	—	—	—	—	—	+	—	—	—	—	—	—	—	—	±	±	+	n	—	+ r	—	6	+	—	—	—	—	+	—	—	ds	?		142
143	B	33	65	?	67	—	—	—	—	—	—	—	+	—	—	—	—	+	—	—	—	p	?	—	—	—	?	?	?	+	+	—	—	—	—	?	?		143
144	D	39	70	68	68	—	+	—	—	+	+	—	—	—	—	—	—	—	—	—	—	+	n	sw	?	lsd	?	?	?	—	—	+	+	—	—	a, ss	nc		144
145	B	41	66	65	60	—	—	—	—	—	+	+	—	—	—	—	+	—	+	—	cd	—	—	—	—	—	?	?	?	+	—	—	—	—	+	—	?		145
146	D	50	82	65	66	—	—	—	—	—	+	—	+	—	—	+	—	—	±	+ l	md	—	—	—	—	—	?	?	?	+	+	—	—	—	—	—	—		146
147	D	39	62	55	?	—	—	—	—	—	+	—	—	—	+	+	+	+	+	+	pd	+	h	sw	+ r	1 + 1	13—19	—	—	—	+	+	+	+	—	ss	?		147
148	E	41	92	70	70	+	—	+	—	+	+	+	—	—	—	—	+	+	+	—	md	—	—	sw	sw	—	10	—	—	+ +	+	—	—	—	+	—	—		148
149	D	42	101	91	95	—	—	—	—	—	—	—	—	—	+	—	—	—	+	+	—	md	—	—	a	—	9	—	—	+	—	—	—	—	—	—	100—60		149
150	D	48	86	62	61	—	—	—	—	+	+	—	—	—	—	+	—	—	—	—	—	md	+ p	n	sw	—	10—7	—	—	+ +	—	—	+	+	+	ra	S 87, nc	mydriasis	150
151	D	38	?	67	70	?	?	?	?	+	+	?	—	—	—	—	?	?	?	?	?	cd	+	n	+ l	—	15—16	—	rnp	+	—	—	—	—	—	—	—		151
152	B	45	85	70	68	—	—	—	—	—	+	+	—	—	—	+	+	—	—	+	+	pd	—	—	—	—	8	—	bnp	+	—	—	+	+	+	ra	?		152
153	D	49	102	64	68	—	—	—	—	+	+	+	—	—	—	+	—	—	—	+	+	spd	—	—	—	—	13—12	—	lnp	+	—	+	—	+	—	—	—		153

1. Number	2. Nationality	3. Age	4. Weight			5. Perlèche	6. Cheilosis	7. Stomatitis	8. Pharyngitis	9. Scrotal dermat.	10. Burning h. & f.	11. Diarrhea	Vertigo			15. Nausea, vomiting	16. Sweating	17. Headache	18. Tinnitus	Hearing loss		Eyes		23. Romberg test	24. Walking test	25. Pointing test	26. Atkinson test	27. Eagleton	28. Perversities on Atkinson test	29. Nystagmus	30. Nystagmoid	31. Praenystagmus	Weakness of		34. Anisocoria	Examination		37. Further particulars	38. Number
			Before war	Lowest	Now								12. Rotatory	13. „Black out"	14. Other forms					19. Subjective	20. Objective	21. Subjective	22. Objective										32. Lateral gaze	33. Convergence		35. Neurological	36. General		
154	D	29	81	39	69	+	—	+	—	+	+	+	—	+	—	+	+	+	+	—	—	bu	—	—	—	12——	+—?	—	+	—	+	—	—	+	—	S 89	pup. irr.	154
155	B	25	70	63	70	—	—	—	—	—	—	—	—	—	—	—	—	+	—	—	spd	p	—	—	—	10—12	—	bnp	—	—	+	+	+	—	—	?		155
156	D	27	78	67	77	—	—	—	—	+	+	+	—	—	+	—	—	—	—	—	spd	+	n	+ b	+ l	sd	10	—	rRb	—	+	—	++	++	—	—	115—70, l		156
157	D	31	69	69	69	+	—	—	—	+	+	++	+	—	—	+	—	+	—	—	—	—	n	—	—	—	6—4	+	—	+	—	—	—	—	+	—	110—55	pup. irr.	157
158	B	23	70	65	65	+	—	—	—	—	—	+	—	—	—	—	—	+	—	—	—	p, la	—	—	—	—	5—8	+	—	—	+	—	+	+	—	—	?	pup. irr.	158
159	D	32	67	60	71	—	—	—	—	—	+	—	—	—	—	—	—	+	—	+	pd	p	—	sw	sw	sd	11——	+—?	rcl l?	++	—	—	+	—	—	a, rl	100—55 o, ST 15		159
160	D	43	76	69	69	—	—	—	—	—	+	+	—	—	+	—	—	+	+ l	+ l	pd	—	?	sw	+ l	sd	20—7	—	—	+	—	—	—	+	+	?	ne		160
	TOTAL					28	11	20	3	37	101	67	39	31	31	62	47	75	56	45			49					26	37	94	67	48	89	74	31				

Comment

1, 38. *Number*: The underlined figures refer to patients described under Case Reports.

2. *Nationality*. From the distribution no inferences may be drawn. There were many technical reasons why Dutchmen preponderated. Statistics on the distribution of the prisoners over the different nationalities are not available.

3. *Age*. The age did not matter very much as is evident from the table. The mean age of English speaking soldiers was on the whole approximately 10 years below that of the Dutch speaking in our camp (25 and 35 respectively).

4. *Weight*. Many patients suffered from serious loss of weight, but this was not a *conditio sine qua non* to develop the syndrome in question. When coming to my policlinic for the first time, most of them had already recovered considerable weight, without having oedema. This is explained, because immediately after establishing a new camp there was always a certain time required to put matters straight, to smooth out several controversies with the Japanese and in the camps proper. In short, it took months before a kitchen was working fairly well, before the prisoners had settled down and established facilities to buy and prepare extra food, etc., etc. A move from one camp to another was a minor, the transfer of a whole camp, a major disaster.

12, 13 and 14. *Vertigo*. In the table only the predominating form of dizziness was given; not infrequently there were combinations between rotational vertigo and black out, and between the latter and rocking or linear sensations of movement. The 101 cases of dizziness were divided in 3 groups according to the predominating complaint.

28, 37. *Reactive past pointing, pupils*. The incidence of mydriasis, deformity of the pupils, and absent past pointing on caloric stimulation in the presence of other reactions is most probably much higher than recorded in these statistics. The reason is that these symptoms were only given attention in the later stages at Bandoeng, thus they could be checked only in some of the patients.

29, 30 and 31. *Nystagmus, nystagmoid, praenystagmus*.

All the symptoms recorded in the table were those as observed during the whole period the patients were under observation. So a patient on the first examination might show nystagmus, later praenystagmus or nystagmoid; also there might be at one moment in one patient nystagmus on looking to the left, nystagmoid or praenystagmus on looking to the right.

36. *General examination*. In this columm only abnormalities possibly having relation to deficiency, are entered.

For the rest the preceding chapters deal with the recorded symptoms.

CASE REPORTS

Some case reports will be given in full. For the sake of briefness only abnormalities are mentioned, as a rule no normal findings. For the method of examination the reader may be referred to the section concerned.

Abbreviations:

y	=	*y*ear(s).
R eye *uw*	=	*r*ight eye *u*p*w*ards.
ALe:h+rN←25—265 (11)	=	*A*tkinson test on *l*eft *e*ar: *h*or. and *r*ot. *n*ystagmus to the right, latency 25 sec., duration 265 sec., quotient 11.
Ro: Re	=	*Ro*mberg to *r*ight *e*ar (dependent on hep).
hep	=	*h*ead *p*osition.
(s)cN	=	(spontaneous) *c*orrection *n*ystagmus.
l eye *p*	=	*l*ateral eye *p*osition.
H	=	*h*earing. Whisper: high frequencies Re *6* Le *5*; low frequencies Re *4* Le *3*; meters.
P	=	*P*olitzer.
Sch (s) r, ml	=	*Sch*wabach (slightly) *r*educed, *m*arkedly *l*engthened.
W→	=	*W*eber to the left.
R+	=	*R*inne air conduction better than bone conduction.
hrN	=	*h*orizontal *r*otatory *n*ystagmus.
wt	=	*w*alking *t*est.
v: +(+) (n)	=	*v*ertigo too marked (very much too marked) (*n*ormal).
pt	=	*p*ointing *t*est.
pp: R=L=n	=	*p*ast *p*ointing R and L *n*ormal.
Neu	=	*neu*rological examination.
Gen	=	*gen*eral examination.
Ophth	=	*ophth*almic examination.
VODS	=	*v*isus *o*culus *d*exter et *s*inister.
g.p.d.	=	*g*rams *p*er *d*ay.
3 mg. i.m.	=	3 *m*illigrams *i*ntra*m*uscular.
Hb	=	*h*aemoglobin, Sahli corrected in %.
wl	=	*w*eakness of *l*ateral gaze.

cw = convergence weakness.
praeN = *prae*nystagmus.
Noid = nystagm*oid*.
bp 105—80 = blood pressure 150 systolic, 80 diastolic.

No. 6. 30 y. 6-3-'43.

History:
14 days ago severe rotatory dizzy spell, with bad headache and sweating. Had burning feet for a short while. 20 cig. a day.

Examination:
Drums: slightly retracted L > R.
Mouth: many carious elements.
Sn ⇆, amplitude ± 4 mm., begins in eye p ± 30° from the middle, nearly pure h, slight r component.

6 6 6 6
H: P:
6 2 6 6

ARe: h + rN → 10—275 (28), Ro: re, pp ←, v: +.
ALe: h + rN ← 10—300 (30), Ro: le, pp →, v: +.

Therapy: Politzer course; dentist. Bellad. 3 × 15 mg. p. d., smoking restricted.
3-4. No improvement, vertiginous sensations remain, with exacerbations now and again.
Therapy: NH_4Cl 2 g. p. d.
29-4. No impr. SN ⇄, and oscillatory hN on looking upward (only in extreme position). Severe headache in many attacks. Coffein-bromural.
20-5. Continuously dizzy, headaches slightly relieved. N ⇆ a little more marked. Sch sr.
Therapy: physostigmine 0,5 mg. s.c. No improvement.
23-5. B_1 10 × 5000 I.U. 3 × weekly, i.m., thereafter 6 × 2500 I.U.
2-7. No improvement. Yeast 20 g. p. d.
30-7. Yeast no longer available. No improvement. Abe as before.
17-9. Anisocoria R > L, mydriasis. Had to go to weavery, dropped out after 5 days.
20-10. Anisocoria gone, N ⇄ marked all the time.
General appearance good, heavily built man. Cw slightly +.
1944 Pakan Baroe. Worked at the railroad, developed typical pellagrous dermatitis of the backs of the hands and feet. Still in rather good general condition.
1945 Pakan Baroe, lost weight enormously, paretic, big tropical ulcer in groin, size of a soup plate, diarrhea, on the verge of death. N⇆, the same characteristics as 2 years ago. Vertigo the same, headaches also. No recurrence of pellagrous dermatitis.
1946 (April) Holland. Put on weight, nystagmus and vertigo nearly vanished, ulcer closed, paralysis improving, is still bedridden.

Comment

Marked bilateral horizontal nystagmus, with slight rotatory component; in the beginning normal hearing, later slight reduction of bone conduction which was taken to be caused by deficiency. Hyperexcitability of both vestibular systems

very marked in regard to the duration of the nystagmus, less so as to the other reactions. The duration of induced nystagmus was difficult to determine in the presence of spontaneous bilateral nystagmus, but observations were made in an eye p not showing sN, ± 15° deviating from the median line. The long duration of the hyperexcitability (March—July 1943 at least) is a central symptom in the absence of otoscopic findings (K l e s t a d t [55]). This is one of the rare cases in which horizontal oscillatory nystagmus was observed.

In Bandoeng, where the majority did not work in the sun, no pellagrous dermatitis developed. In Pakan Baroe with work at the railroad this symptom appeared, to vanish again when the patient was too weak to work outside and remained in hospital.

No. 14. 46 y. 24-3-'42.

History:
A few months ago on rising in the morning suffered severe vertigo, had to clutch for support to avoid falling. This occurred immediately on bringing the head in upright position. Slight nausea. Every morning the same. Handled machine guns for years and years without ear protection. L. drum ruptured by a blow in youth.

Examination:
Drum L: scarred antero-inferiorly.
CN in both 1 eye p. These positions difficult to maintain, marked diplopia → > ←. Cw ++. Typical staring gaze. Muddy complexion.
Ro: sw + inclination → Falls once →.
Pt: both arms →.
Wt: for- and backwards definitely ← (no particulars to be found on legs and hips).

2 0.80
H: P: no marked effect, W: n, Sch r.
2 0.80
(Sat always with left ear towards muzzle of machine gun).

ARe: h + r N → 20—230 (12), Ro: re, no pp, v: +.
ALe: h + r N ← 18—250 (14), Ro: le, pp: n, v: ++.
Gen: L 5100. Hb 90 %.
Ophth: hyperaemia of optic discs. VODS 5/9.
Therapy: 3 eggs a day.
23-4. ScN ← only.
22-5. Dizziness now occurs consistently in supine position, also on examination, but no nystagmus. However, the eyes float slowly back from l eye p, nearly to central position, go back with a jerk, irregular: Noid ⇄.
4-8. VOS 5/6 VOD 5/9. Noid ⇄. Wl more marked, cw ++.
Dizziness decreased. Patient turns round in bed over the belly, to avoid the supine hep.
3-9. Had 3 eggs a day all the time. VODS as before, the rest also, only dizziness increased again.

Comment

A patient with marked staring gaze through extreme weak convergence and lateral gaze. The l eye p cannot be maintained, the eyes are dragged back nearly towards the middle line. Positional vertigo, at the outset on upright hep (not lasting), later in hep backwards. There is dissociation between on the one hand pt and Ro → and on the other the wt ←; there is hyperexcitability on both ears for all components, except for pp on the R e, which failed to occur; all of them symptoms definitely pointing to the central vestibular area.

No. 18. 29 y. 9-3-'42.

History:

For some weeks attacks of slight rotatory vertigo, sometimes with sickness. Occasionally sick without dizziness. Severe burning feet. Slight continuous headache. Swelling of nasal mucosa alternating R and L. 10—15 cigarettes a day.

Examination:

Nasal mucosa R swollen.
Mouth several teeth missing.
Ro: swaying, falls once ←.
Wt: unsafe, twice ←.
CN in both l eye p, fairly long, ± 15 beats each.
Lp difficult to maintain, becomes sick.

6 6
H: , P: no improvement. Sch sr.
4 4

ARe: h + rN → 25—265 (11), Ro: Re, pp: R = L = n, nausea, flushed face, slight sweating, v: +.
ALe: h + rN ← 25—220 (9), Ro: Le, pp R = L = n, v: n.
Neu: hyperaesthesia skin of arms and legs. Deep sensibility slightly disturbed.
Gen: Bp 105—80. Leuc. 5400. Narrow capillaries of fingers and toes. Got 7 × 1 mg. B_1 i.m. there without alleviation of complaints.

Therapy: 10 × 25 mg. B_1 i.m. 3 × weekly.

3-5-'42. Headache gone, rest as before. Dizziness decreased in number of attacks, increased in intensity. Whilst walking sensation of swaying, when sitting sometimes turning vertigo; when sleeping sometimes to and fro movements of the bed, sometimes dreams of being tied up to a propeller. Clutches for anchorage, nausea on the verge of vomiting, palpitation and acceleration of pulse.

ShrN in both l eye p → > ←, weakness of lateral gaze.
Marked increase of N → in right lateral hep.
,, ,, ,, N ← ,, left ,, ,, .
Diplopia in both l eye p.

Therapy: Solutio Charcot cum chloral hydrate.

21-6-'42. Had attack of benign tertian, quinine. More deaf.

4 6
H: Sch r. Anisocoria.
3 4

13-9-'42. Benign tertian again. Hb 80 %. Admission to hospital.
13-10-'42. Discharge. Got considerable extra animal protein and sometimes liver in hospital. Dizziness decreased.
ShrN → > ←. Hb 102 %. A tests approximately as before.

Comment

A young man with nearly continuous vertiginous sensations, with occasional severe dizzy spells of rotational character. Linear and rocking movements are also present. The hyperexcitability, on the R ear for all components (N, vertigo, vegetative sensations), on the left for the duration of N only, is a central symptom in the presence of normal middle ears, and on account of its long duration. The slight bilateral perception deafness (probably caused by deficiency), the bilateral hrN, and the positional N of Nylen's type II fit in a central picture. The wl, the anisocoria, the dissociation between Ro and wt ← on the one hand and normal pt on the other, positively point to the brain stem.

Strange is in this case the Ro, influenced by the l eye p which also evoked dizziness. Kuilman [65, 66] describes an analogous symptom. The backward falling on converging in my opinion must be explained as the result of an effort of a patient with unsafe balance in the Ro position to alleviate convergence. This was often observed. The other symptom Kuilman describes, inclination ← on looking → and inversely, I never saw. This patient is the only one I saw, who fell backward in l eye p.

A cN, observed in the earlier examinations, later became a lasting one. There is a discrepancy between the vertigo and the N, the former decreasing, the latter appearing in the course of time, which again is common for central affection and not seen in peripheral disturbance.

No. 21. 47 y. 14-6-'43.

History:

Became dizzy 14 days ago, after a day of work in the weavery. Slight nausea. 10 days ago severe tinnitus in both ears. Became a little deaf in camp. Vertigo: rotational, sensation of swaying when walking. Burning hands and feet. One son died in another camp, got message 1 month ago. Weight 73—59—62.

Examination:
Drums: slightly retracted.
Nose: swollen mucosa L. Crista septi R.

2	2	5	5	
H:		P:		W ←, R +, Sch sr.
2	2	4	4	

Wt: sw, more →.
Pt: la →.
Ro: sw, inclination →, falls once →.
PraeN ⇄ in bl eye p ← > →. No influence of hep. In this position marked diplopia (crossed), slight pain, lacrimation, position difficult to maintain.
ARe: hN → 25—310 (12), rN very little marked, but present; v: +, Ro: re, pp as above, nausea, profuse sweating.
ALe: hN ← 25—285 (11), Ro: le, rN, pp and other reactions as above.
Neu: sN ← Diplopia in l, uw gaze and in convergence. Reflexes aggravated. 1st and 2nd toes hypaesthesia.
Gen: capill. fingers and toes narrow. Leuc. 6500, Eos 10 %.
Therapy: 2 eggs, peanut butter, blood sausage.
7-7-'42. Cw marked now. SN ← praeN →. Admission to hospital.
7-8-'42. Discharge. Subjectively better, objectively *status quo ante*.
10-9-'42. Noid ← cN →. Abe as before on the whole.
August '44 torpedoed on prison ship, was 2 days in water, arrived in Pakan Baroe.
Gait spastic paralytic, slight oedema of the legs.
SN ⇄. Cw very marked, lw also.
Died a few months later with complete Korsakoff syndrome.

Comment

One of the cases where the weavery probably brought the dizziness out, that is, caused the overflowing of the bucket. The death of his son probably influenced the avitaminosis adversely by sorrow and grief. This is an additional factor which was frequently met in beriberi in soldiers in peace time. They were not infrequently observed to develop beriberi when imprisoned, while receiving the same food as before. This may be explained by decreased food intake and diminished secretion of digestive juices (follow Pavlov's notorious experiments [90].

The weakness of lateral gaze and of convergence, the nystagmus, vertigo and bilateral tinnitus may all be explained by a brain stem lesion. Past pointing is not influenced by 1 cc. cold water, direction of Romberg and nystagmus is. The hyperexcitability of the signs, covering all symptoms (except pp), are central signs. Additional affection of both VIIIth nerves cannot be excluded. The slight perceptive deafness remaining after tympanal inflation was taken to be a presbyacusis, although the tinnitus, occurring with the vertigo, is suspect.

A praeN in both l eye p in the course of time grew to a sN (occurring immediately) in these positions.

No. 30. 44 y. 31-5-'43.

History:
Diarrhea 6 months ago, recurring again 3 weeks ago. Difficulty in walking, swerves right and left. Hearing acuity diminished in camp. Profuse sweating. Had perlèche, glossitis and scrotal dermatitis. Headaches. Weight 76 — 62 —?
Examination:
Nose: deviation + crista septi →.
Ro: sw. Pt: deviations in several directions.
Wt: falls, not possible to carry out.

5	4		
H:		P: no improvement (tuning fork tests illegible).	
2	2		

CN ⇆.
L eye p difficult, diplopia, very dizzy, profuse sweating. Convergence possible to normal extent, however, ataxia of this movement on moving a finger from and towards the eyes. Very dizzy, sweating. Convergence spasms occasionally. Gets this hereafter also when looking laterally; when beginning with lateral gaze, however, only weakness thereof.
ARe: Falls like a statue from chair. V + +, soaked with sweat, looses consciousness for a moment.
Neu: reflexes aggravated, marked ataxia, legs and arms pale-cyanotic, sweating, superficial sensibility of both legs diminished sockwise.
Therapy: 3 eggs a day.
Gen: Hb 91 %. L 4500.
2-6. VODS 5/18 (on 31—5 normal). Admission to hospital. Had Pick's visions whilst reading; a block of letters came out of the line and stood obliquely above it, came back again. This several times on consecutive days.
5-9. Anisocoria L > R. Convergence all right.
Noid ⇄, wl +.
11-10. Noid ⇄, wl +. Ataxia of convergence again.
VODS 5/9. Scotomata.

Comment

A patient with marked ataxia of arms, legs, body and even of the eye movements. This occurred in convergence only; but once the balance of the eye muscles was thus disturbed, also on lateral eye movements, and consisted of convergence spasms or over- and underdosing of convergence. Wl marked.

Possibly in this patient there was abolition of the quick nystagmus phase. The visions of Pick are seen in lesion

of the posterior longitudinal bundle from disturbance of coordination between ophthalmostatic and vestibular impulses (B i n g [13]). The wl may easily be explained by the same lesion. The underlying pathology of the anisocoria and ataxia of convergence must lie in the brain stem as well. Later he developed nystagmoid eye movements, unfortunately I am not able to discover from the records if this was one of the patients showing spontaneous group forming in nystagmus. Certainly there was a slow dragging back of the eye balls from the lp, with recovering jerks; the rhythm, however, was not recorded.

No. 38. 27 y. 22-5-'43.

History:

Ophth: retrobulbar neuritis, VODS formerly 5/10, now 5/6. Sent over to me because of sN.

Slight vertigo, especially on rising in the morning, rotational. Slight headache, both are more or less continuous. 10 cig. a day. Weight 80, 67, 69.

Examination:

ShN ⇄. No influence of different hep.

C possible in normal degree, but evokes slight dizziness.

Wt: forward ←, backward normal.

ARe: h + rN → 15: 275 (18), Ro: re, pp: n, nausea and sweating marked.

ALe: h + rN ← 15: 230 (15), Ro: le, pp: n, other reactions as on Re.

Muddy complexion.

Neu: finger — nose test R disturbed. Wt ←.

Therapy: Had 3 eggs a day for one week. Smoking restricted.

11-6. ShN ⇄ less marked. Complaints (headache, vertigo) decreased, but not abolished. Photophobia.

3-9. SN gone. Still slight complaints. Extra food changed to blood sausage.

$$H: \frac{6\quad 6}{4\quad 4}, \quad P: \frac{6\quad 6}{6\quad 6}, \quad \text{Sch sl.}$$

Vasomotor rhinitis, trichloracetic acid applied to mucosa.

14-9. Abe 16, concomitant reactions as on 22—5.

SN ⇄ present again, still a bit dizzy on converging, spontaneously not.

1944, Batavia (Febr. or Apr.). Gets severe dizzy spell when bringing head or body and head in R lateral position, with vomiting, nausea and sweating. He scrupulously avoids this position.

Examination: When bringing the head in R lateral position after a few seconds latency 3rd degree hN →. Another position is immediately assumed, the N then subsides in the course of a few minutes to zero. Vomiting, sweating, pallor, palpitation. Drums, hearing normal, no sN.

This phenomenon, tested once a day for several consecutive days, remained for about one week, diminishing in intensity. The position from which was started to obtain the critical one, and the hep with respect to te body were immaterial, it was the hep with regard to the gravitation that elicited the attack.

After one week contact with this patient was lost.

Comment

A case with many central-pointing symptoms: the little marked, nearly continuous, vertigo in the presence of shN ⇄ and normal hearing; the long standing bilateral hyperexcitability in the absence of otoscopic findings. This is one of the cases in which the sN vanished and reappeared during the period of observation; the vertigo did not parallel this objective phenomenon, on the contrary. The discrepancy between sN and vertigo is a central symptom again. Later a very marked positional nystagmus + vertigo of N y l e n's type I.

This case had no wl, which makes a paretic gaze N improbable.

No. 133. ± 28 y. 21-8-'43.

History:

Has had perlèche, stomatitis, photophobia and burning of conjunctivae for ¾ year. Had burning hands and feet. Diarrhea ½ year ago severe, improved slowly, not yet completely gone. Vertigo started ¾ year ago, did not improve, especially after exertion, consists mainly of "black out" with profuse sweating, accompanied by slight rocking movements. On exertion of the eyes he gets frequent headache. 6 cig. a day. Weight 86, 60, 78, 74.

Examination:

Drums: slightly retracted.

Nose: spina septi →.

Mouth: perlèche, glossitis at margins and tip. Dental tartar. Gingivitis.

Wt: slightly ←.

ShN ⇄ in both 1 eye p. Closes eyes convulsively at once. Lacrimation, pallor, sweating, dizziness, even without reaching extreme position. Cw +.

On looking → the R eye turns upwards, ± 0,5 cm.

In L 1 eye p diplopia vertical and horizontal, in R 1 eye p horizontal only. On covering L eye, all movements possible on R one.

ARe: hN 25—150? (6?), Ro: falls to Re, severe nausea and sweating, feels ill, no rotatory N to be provoked in hep 60° backward and 45° to the L, no pp, v: + +, expiration of induced N difficult to determine through convulsive attempts to close the eyes. Completely limp.

Ophth: nightblind.

Neu: reflexes aggravated, vasomotor lability.

Therapy: 1 egg + blood sausage + yeast 20 g.p.d. Dentist.

22-9. No appetite. Lost weight again. Nausea and occasionally vomiting, sometimes when lying down.

4-12. The vertical deviation is less marked. Patient feels slightly better. Counterrotation was not tested.

Comment

One of the 2 observed cases of H e r t w i g-M a g e n d i e's deviation. The R labyrinth was very much hyperirritable in

all components, with as striking contrast the unexcitability of the rotatory pathway and that for past pointing, whereas the Romberg was very markedly positive again. The other ear was not tested because of the severe reaction. Observations were difficult for the same reason, therefore the positive Eagleton was not counted in the table. The duration of the induced N probably was much longer also, but the patient became very sick by looking only a little laterally. With, finally, the normal hearing, a complete central vestibular picture.

Concomitant signs of avitaminosis on lips, tongue and in the digestive tract.

Interesting is the double indication of affection of the rotatory pathway: Hertwig Magendie's deviation on looking to the L, and positive Eagleton's symptom on cold stimulation (Muskens, Aubry[4]).

No. 7. 38 y. 7-3-'43.

History:

In July '40 (i.e. 2 years before captivity) for the first time severe attack of rotatory vertigo with nausea, sweating and tinnitus on L e. Became deaf on this ear. Complete disappearance of the vertigo required a week or two. Was treated for narrowed Eustachian tube L. In August '42 (i.e. 5 months after being interned) a second attack whith relapse before complete disappearance of the symptoms of the preceding one. In December free, in January a new attack again, the vertigo was not yet vanished at the time of examination. 30 cig. a day.

Examination:

Nose: slight septal deviation →.

Pharynx: considerable amount of pus can be squeezed out of both tonsils.

Nasopharynx: adenoid, small.

H.- 6 2 Catheter: L slightly narrowed, no improvement. 6 ad c

W: ←, Sch Le r.

ARe: h + rN → 35—150 (4,3), no other reactions.

ALe: h + rN ← 90— 30 (⅓), „ „ „ .

Gen: no particulars (a few weeks ago), got belladonna, no improvement.

Therapy: Catheter course, NH_4Cl, smoking restricted.

7-4. Much better, though not yet vanished.

7-5. Complaints not vanished, on the contrary they are increasing again a little. Cn ←.

Comment

A patient with fully developed Ménière's symptom complex, one attack before the war. In captivity the attacks,

less severe, came much more frequently, and the symptoms tended to remain in the interval. There is slight or no increase of Atkinson's quotient in the right (normal) ear, a marked decrease in the affected ear. No nystagmus or other objective vestibular symptoms. This is one of the patients who drew our attention to the vertigo, one of a group of 4, all old sufferers from Ménière, who developed more attacks in camp life. The lesions here certainly were peripheral: unilateral deafness, hypoexcitability of the ear affected since a considerable time.

However, to our astonishment, more and more central pictures were found, so that the presumption arose that also in the cases with certainly peripheral affection, stimuli from the periphery were potentiated in a hyperirritable central vestibular area and thus gave rise to more frequent attacks. In this patient there are no central-pointing symptoms, except perhaps the hint given by the character of the vertigo (inclination to less marked attacks and persistence of the symptoms in the interval).

A correction nystagmus was found in the last examination, only to the good ear, with increase of subjective symptoms. The unilateral deafness was taken to be of perceptive type, peripheral.

CHAPTER IV. LOCALIZATION

A. ANATOMY

The VIIIth or *acoustic nerve* consists of two branches, the *vestibular* and the *cochlear*. The latter is (with its corresponding part of the labyrinth), phylogenetically the youngest and most vulnerable. Both sections are sensory and composed of fibres having their respective ganglia outside of the central nervous system, in this case in the temporal bone. They are completely comparable then to the sensory fibres of the cord's dorsal roots. The vestibular nerve has a proprioceptive, the cochlear an exteroceptive function. Both sets of fibres enter the brain stem at the boundary between medulla and pons. Here they separate and synapse with the *vestibular* and *cochlear nuclei* respectively.

Table showing subdivisions of the brain

(modified from a table of Ranson[99]).

	Primary vesicles	Subdivisions	Derivatives	Lumen
Brain	Prosencephalon (forebrain)	Telencephalon	Cerebral cortex Corpora striata Rhinencephalon	Both lateral + rostral portion of 3rd ventricle.
		Diencephalon	Thalamus	3rd ventricle.
	Mesencephalon (midbrain)	Mesencephalon	Corpora quadrigemina Crura cerebri	Cerebral aquaeduct.
	Rhombencephalon	Metencephalon	Cerebellum Pons	4th ventricle.
		Myelencephalon	Medulla oblongata	

Cochlear nerve: This nerve consists of fibres from the *ganglion spirale* Corti. These fibres synapse with the *dorsal* and *ventral cochlear nuclei*, from which the second neurons for the greater part decussate. Both sets of fibres, crossed and uncrossed, run rostrally in the paired *lateral lemniscus*. These fibres terminate in the *inferior colliculus* (*corpus quadrigeminum inferior*) and the *medial geniculate body* (*corpus geniculatum mediale*). The latter is a way-station on the auditory path to the cortex, the former is a reflex-centre.

The fibres in one lateral lemniscus then for the greater part originate from the contralateral ear; the minority is coming from the homolateral one.

Vestibular nerve: The fibres take origin from the *ganglion vestibulare* Scarpae. Its fibres end in *4 vestibular nuclei* and in the *cerebellum*. The 4 vestibular nuclei are:

1. The *medial, principal, triangular* or *dorsal vestibular nucleus* of Schwalbe, the largest, partly in the pons, partly in the medulla.

2. The *spinal* or *descending vestibular nucleus* of Roller, lying in the rostral part of the medulla.

3. The *superior vestibular nucleus* of Bechterew, in the pons, at the level of the abducens nucleus.

4. The *lateral vestibular nucleus* of Deiters, caudally in the pons.

All four nuclei lie in the floor of the 4th ventricle. The spinal, superior and medial vestibular nuclei give rise to a set of fibres, running through the paired *medial longitudinal fascicle* (or *posterior longitudinal bundle, fasciculus longitudinalis medialis* s. *posterior*). The fibres either cross or not and run either up- or downward. Fibres coursing rostrally go to the motor nuclei of the ocular muscles in the mesencephalon. The descending fibres terminate in the nucleus of the spinal accessory nerve and in the anterior column motor cells of the cervical portion of the spinal cord. Thus reflex arcs are established from the labyrinth to the eyes and to the neck muscles.

A second set of second neurons originate from Deiter's lateral nucleus, descending in the homolateral anterior funiculus

of the cord, as *vestibulo-spinal tract*, subserving reflex control of (neck?), arms, body and legs.

Up to this point there is agreement between the different investigators, so far I can see. There is no agreement as to the number and type of crossing and uncrossing fibres.

The part of the cortico-bulbar tract subserving conjugate lateral eye movements, the fibres of which are axons of motor cells at the foot of the 2nd frontal convolution, courses through the genu of the internal capsule and the cerebral peduncle to the brain stem and decussates, to end at the motor nuclei of the extraocular eye muscles. Most of the authors agree, that these fibres are coursing in the posterior longitudinal bundle (after decussation); the point of entrance in this bundle, however, is not known. Spiegel states they synapse with the vestibular nuclei, as he proved in the cat [116]. In any case these fibres have to fuse with the vestibulo-ocular ones in some way and in some place. Some authors assume a *supranuclear intrapontine centre for conjugate gaze*, very near the VI nucleus [55, 116].

Summing up, we know there is a connection between the vestibular nuclei and those of the extraocular eye muscles through the posterior longitudinal bundle. Most probably the fronto-ocular tract is fusing with this bundle. The former's section between the cerebral peduncle and the nuclei of the ocular muscles, however, is not exactly known. Whilst the one states that these fibres are the same as the vestibulo-mesencephalic ones, the other only assumes a close proximity of both systems in a short section between the vestibular nuclei and those of the eye muscles (respectivily the pontine centre for lateral gaze). This section is the posterior longitudinal bundle.

In disturbance of this final common path of fibres afferent to the extraocular eye muscles a paretic nystagmus is the same as a vestibular one, according to Klestadt [55]; this nystagmus has the characteristics described in chapter II.

The brain stem is primarily a great junction and connecting pathway between cerebrum, cerebellum and spinal cord, where all afferent and efferent nervous impulses have to pass. In this situation we have observed the *posterior longitudinal bundle*

as a pathway of extreme importance, as moreover stressed by its existence in all vertebrates and its priority in myelination, namely in the 4th—7th month of intrauterine life. Rostrally the bundle seems to originate from the paired *nucleus of the posterior commissure* of Darkschewitsch, decussates in this commissure, swings along the side of the ventricular wall, hugging the paired oculomotor nucleus. At this level the bundle is in relation with the paired *nucleus interstitialis* of Cajal. From here it maintains a median and dorsal (posterior) position, near the floor of the cerebral aquaeduct and immediately at the floor of the rhomboid fossa, to be crowded from its place only by the decussating pyramidal fibres. Apart from the sets of fibres discussed above, the bundle contains fibres from the IIIrd nucleus to the neurons of the facial nerve supplying the orbicularis oculi and corrugator supercilii (see eyelid nystagmus).

Oculomotor nucleus (III). This nucleus is paired, lying upon the posterior longitudinal bundle, between this and the central gray matter surrounding the cerebral aquaeduct, at the level of the superior colliculus. It innervates the extrinsic eye muscles. There is a median, unpaired mass of cells between them, *Perlia's nucleus*, taken to be the *centre for convergence*. Between the left and right oculomotor nuclei lie the paired *nuclei of Edinger-Westphal*, held to furnish the fibres to narrow the pupils.

Trochlear nucleus (IV): This paired nucleus has the same position with respect to the posterior longitudinal bundle as the IIIrd, only at a more caudal level, that of the inferior colliculus, close to the caudal extremity of the IIIrd nucleus.

Abducens nucleus (VI): This is the most caudal one, paired, in the floor of the 4th ventricle, at the same level as the facial nerve nucleus and the rostral end of the vestibular nuclear mass. It lies closely on the lateral side of the posterior longitudinal bundle.

These anatomical facts are compiled from Ranson [99], Cunningham [26], Piersol [92], Spatz [116], Aubry [4] and Klestadt [55].

B. COMMENT ON NYSTAGMUS

We have on purpose refrained from making a comment on nystagmus in the chapter of symptomatology, because this would take too much space there. In considering the other symptoms, we frequently had opportunity to conclude that there were many symptoms pointing to the brain stem, many others that did not put a brain stem lesion out of court, and little that pleaded for a peripheral lesion.

The characteristics of a nystagmus of central origin as such will now be enumerated and compared with those of the nystagmus in our patients, in which we shall have to be satisfied with examination without spectacles of Bartels or Frenzel.

1. Nystagmus with a pure plane of beating (i. e. either horizontal, or rotatory, or vertical), is more probably of central than of peripheral origin. The rotatory nystagmus is elicited from the caudal part of the vestibular nuclear area, the horizontal form in the rostral part up to the abducens nucleus level. Above this point vertical nystagmus may be elicited, especially the commissural area is apt to give this sort of nystagmus, which nearly always is central when spontaneous (Leidler[69], Aubry[4], Klestadt[55]). Pure planes of beating in peripheral spontaneous nystagmus may be expected only in isolated affection of one canal, and then either horizontal or rotatory, never vertical[55]. In our patients in the greater part of the 94 showing spontaneous nystagmus, this was purely horizontal. Second in incidence was the horizontal rotatory form. Other forms were not seen.

2. Long standing spontaneous nystagmus is another symptom pointing to the central vestibular area. Peripheral nystagmus is always diminishing in all qualities. Even when remnants of a distinctly decreasing nystagmus remain for weeks or months, this is already suspect for central origin. Peripheral nystagmus is always waning whilst the cause may be persisting; whereas central nystagmus tends to persist as long as its cause[55,4]. There were many patients with long standing nystagmus, more than half of the total number.

3. A third point for a central situation is discrepancy between

the intensity of the nystagmus and the subjective sensations[5, 17, 55, 4] etc. This discrepancy was a quite common symptom in our patients.

4. Irradiation of the nystagmus eliciting impulses on nerve fibres supplying other muscles of the face or neck is suspect for brain stem affection[55]. An eyelid nystagmus was not infrequently observed; I am not able to give statistics.

5. If in multiple or bilateral nystagmus the eyes do not always reach the extreme position, even when leading them with a moving object, central origin is nearly certain: affection of the supranuclear pathway[55] (= the posterior longitudinal bundle).

A nystagmus elicited in the vestibular nuclear area by irritation, beats to the affected side, one evoked by destruction to the sound side[5, 55, 4].

In the posterior longitudinal bundle Klestadt assumes destruction as the only possibility, because no „energy providing" ganglia are present there[55]. Aubry is of another opinion and distinguishes between irritative and destructive lesions also in this bundle[4]. There is no agreement in the literature as to the decussations of fibres in this tract, most authors, however, agree that a destructive lesion of one posterior longitudinal bundle may evoke nystagmus to the affected side[142, 13, 55]. If irritation is possible, the nystagmus will then beat to the sound side. Thus there is a reversal of direction as compared with the nuclear area, which could mean decussation of the greater part of the fibres. In the small dimensions in this region, and in our ignorance of the exact course of the different sets of fibres, conclusions as to further localization of lesions within the central vestibular area are often more or less speculative.

Weakness of lateral gaze, present in 89 patients, was in 42 cases correlated with nystagmus. In most cases the nystagmus was beating to both sides, however, mostly more marked to one side. Apart from the fact that inferences as to the side of the lesion are more or less dangerous, we must consider that this disease is no neoplasm or circumscribed inflammatory product, but more in the class of an encephalitis or disseminated sclerosis (see below).

6. Nystagmus in people with normal hearing is more suspect for central, than for peripheral origin. In the peripheral area the vestibular and cochlear parts of labyrinth and VIIIth nerve are close together, in the central area less so [142, 5, 13, 55, etc. Nystagmus in patients with normal hearing was found in 23 of 33 cases, a conspicuously high incidence. Moreover in 10 out of 19 patients with conduction deafness a nystagmus was observed.

7. There is a tendency in the literature to regard a positional nystagmus as a central, rather than a peripheral symptom [17, 69, 4].

Positional nystagmus was only infrequently tested for; once Nylen's type I, twice type II was encountered (see table column 37).

There were 21 cases with nystagmus showing big amplitude and occurring in an eye position not far from the middle line, which showed no nystagmus in straight ahead gaze. These showed a rapid declination of amplitude then from lateral to middle eye position, which is characteristic for paretic nystagmus. However, these observations were made without excluding fixation, part of them might have shown nystagmus in the middle position as well, if Frenzel's spectacles had been used. Of these 21, 11 showed no difficulty in reaching the extreme lateral eye position, especially for these perhaps a vestibular origin might be assumed, in which case the nystagmus certainly would have been 2nd degree behind Frenzel's spectacles. The remaining 10 showed concomitant weakness of lateral gaze, and here, a paretic nystagmus is probable, localized in the posterior longitudinal bundle or even higher up in the fronto-ocular tract (see pathology). In many of them there were certainly correlating symptoms pointing to the brain stem. In this disease we must, however, try not to localize disturbances too exactly, because it tends to affect the whole central nervous system, certainly with some places of predilection which are more severely degenerated.

The same reasoning may be applied to the other nystagmus cases, less marked, and numbering 73. Of these 32 showed accompanying weakness of lateral gaze, paretic nystagmus being probable. For the remainder vestibular nystagmus,

elicited in the vestibular nuclear area (horizontal or horizontal rotatory form!) is probable. Mixed forms of paretic and vestibular nuclear nystagmus are quite possible and even probable, as Cords also assumed in disseminated sclerosis [39].

There was one patient with 3rd degree (positional) nystagmus in this group, and 2 were observed with 2nd and 3rd degree nystagmus outside this group; these 3 cases undoubtledly had nystagmus of vestibular origin.

C. SEARCH FOR PERIPHERAL SYNDROMES

We were quite astonished in the beginning to find little peripheral and many central syndromes, through having taken notice of Selfridge's publication on demyelinization of the VIIIth nerve caused by avitaminosis [109], and similar communications in the Year Book of Eye, Ear, Nose and Throat 1940 [14].

Considering unilateral deafness and to a lesser degree unilateral hypoexcitability of the labyrinth as peripheral symptoms, and looking from this point of view through the table, we come across no. 7, 11, 36, 67, 85, 109, 112, 116, 118, 128 and 130. In all of them, except the first two, we will find many centrally pointing symptoms, which does not exclude additional peripheral lesions. A harmonic peripheral picture, on its way from the labyrinth or nerve to the different organs, is distorted, dissociated and rendered dysharmonic in the affected brain stem, through which the impulses have to pass. The same reasoning appertains to other patients in which no peripheral signs at all were observed, a peripheral picture may not come through as such from disturbance in the brain stem. This is no theoretical reasoning, as will be seen in the pathology. Secondly we must consider that bilateral peripheral lesions of approximately the same degree are apt to give a more or less ambiguous picture. In avitaminosis a bilateral affection is on the whole to be expected.

Patient no. 7 is described in full, as no. 11 a case showing complete Ménière's syndrome before the war, with increase of number and intensity of the attacks after a six months stay in the camp. Both showed no central symptoms, except

perhaps no. 11 the hyperirritability in the sound ear. A hyperirritable central vestibular area would account for increase in the number of attacks: small stimuli from the periphery, under normal circumstances not giving rise to an attack, are reinforced on their way through the central area and thus elicit an attack. In the camp quite often, much more than normally, patients with tubal obstruction were observed to develop nystagmus and vertigo which often subsided on tympanic inflation. The same explanation holds for the latter cases.

On looking through the table from other points of view to find peripheral pictures, we will search in vain and come no further than the cases no. 7 and 11. Again, surely there were many more peripheral lesions, but the symptomatology of these was irrecognizably mutilated by additional central disorder.

D. SUMMING UP OF LOCALIZING VALUE OF ALL SYMPTOMS

Hyperexcitability (118 cases) is a central symptom. K l e s t a d t writes: "To localize hyperexcitability peripherally, it is nearly necessary to demand correlating otoscopic findings, so rare is peripheral origin. Certainly hyperexcitability may be peripheral in initial phases, practically only paralabyrinthitis can produce it" [55].

The *nystagmus* (94 cases) is considered to be due to lesion of the central vestibular nuclear area in the greater part of the cases; in the other part to lesion of the fronto-ocular tract (nystagmus in paretic gaze), probably in the posterior longitudinal bundle. The same applies to *weakness of lateral gaze* (89 cases). Mixed forms of nystagmus are not improbable.

Some of the cases with *nystagmoid* (total 67 patients) showed *nystagmus with group forming*, which is characteristic of a lesion in the posterior longitudinal bundle.

Eyelid nystagmus is a sign of irradiation of impulses to the facial nerve, probably from the posterior longitudinal bundle.

P i c k's visions (2 cases) and *H e r t w i g-M a g e n d i e's deviation* (2 cases) are also localized in this fascicle.

The *weakness of convergence* (74 cases) is most probably a mesencephalic symptom (P e r l i a's nucleus).

Spontaneously *positive R o m b e r g test* (60), *walking test* (74) and *pointing tests* (57) are considered to be evoked in the central nervous system because of their mutual dysharmonic character.

Reactive vestibular dysharmonies and *dissociations* are in all forms and by most authors considered to be central, especially when syphilis can be excluded. This concerned *E a g l e t o n's symptom* 26 times and other abnormalities on cold stimulation 42 times. Abnormalities in induced past pointing are attributed to the vestibular nuclear area and immediately caudal therefrom.

Anisocoria (31 cases), *mydriasis* and *deformity of the pupils* do not contradict central lesions, (E d i n g e r-W e s t p h a l's nucleus in the mesencephalon).

The *vertigo* in the greater part of the cases (total 101) had more a central than a peripheral character.

The *deafness* (42) and *tinnitus* (23 cases) were nearly always bilateral, which makes a central cause possible.

B i n g's ocular cogwheel sign was not infrequently observed. This is certainly dependent upon lesion of the central nervous system, probably of the extrapyramidal system.

Ataxia of convergence (6 cases) is a central nervous symptom. In the *neurological examination* there were some symptoms pointing to the central nervous system, some pointing to the peripheral nerves, and many that did not rule out central lesions.

There were only 2 cases of 160, in which there was a more or less clearly cut peripheral oto-neurological picture.

E. OTO-NEUROLOGICAL PICTURE

This disease has a characteristic oto-neurological picture, markedly different from that in other diseases. It is most similar to that of *disseminated sclerosis*, which is not surprising when it is remembered that the brain stem is one of the places of predilection in both diseases. A u b r y examined a great number of patients oto-neurologically and laid down his

findings in a book to which repeated reference has been made. Among these patients were 181 with multiple sclerosis [4]. A summary of his findings, as compared with ours in avitaminosis, will make clear the great similarity and the points of difference between both disease pictures.

	181 cases of multiple sclerosis (Aubry [4])	160 cases of central nervous system disturbance in avitaminosis
Vertigo	frequently	101 cases, 63 %
Nystagmus	60 %, rarely unilateral, nearly always horizontal, mostly multiple	59 %, mostly horizontal, bilateral, no multiple nystagmus
Oscillatory nystagmus	1 %	2,5 %
Positional nystagmus	1 %	2 % (?)
Spontaneously: Romberg, walking, pointing normal	46 %	39 %
Hyperexcitability	28 %	74 %
Eagleton's symptom	20 % (3 tests)	(caloric test only) 16 %
Diplopia	22 %	71 cases, 44 %
Deafness	Rather rare and light, quite variable	26 %, constant

Hyperexcitability was the most frequent symptom in our patients (74 %), the disease which comes next in this respect is multiple sclerosis with 28 %. It must be borne in mind that our patients form a group with oto-neurological disturbances selected from avitaminotic patients. From this picked group 74 % showed hyperexcitability. The same applies to all statistics, as was pointed out before. For the rest hyperexcitability is a rare finding in the oto-neurology.

Diplopia in multiple sclerosis in the presence of vestibular signs is regarded to be of vestibular origin by Barré, it is considered to be a disturbance in conjugate movements of the eyes [4]. Aubry and Ombredanne agree, having noted the same symptom after section of the VIIIth nerve for four to five days [4]. In our patients vestibular origin is quite possible, though in most of the cases weakness of convergence may account for the diplopia.

Aubry writes on multiple sclerosis: "The diffuse affection

of the brain stem entails quite varying vestibular pictures, which on the whole give the impression to be superficial, that is to say more *irritative* than destructive" [4]. We could apply this same sentence completely to our group of patients. "*Ce sont des lésions qui lèchent, mais qui ne mordent pas*" [4] (at least in the beginning).

The *variability* of the symptoms is still more obvious in disseminated sclerosis than in our disease.

There are more points of resemblance between the two: the liability to remissions and exacerbations, the retrobulbar neuritis, the inclination to affect fibres rather than nuclei in the central nervous system, and the tendency to be misinterpreted in early cases for hysteria or neuropathy. Of course there are many points of difference [112, 13, 54, 45, 129]. Still, there is a trend in the literature to look at multiple sclerosis from a nutritional point of view (Brickner and Brill [15], Moore [81]). For the moment I think we are entitled to state that certain forms of multiple sclerosis, and especially in early stages, may be very similar to such of avitaminosis, or even undistinguishable from them. Concomitant digestive tract or skin lesions make the diagnosis certain; if not present (also in the previous history!), the weight of evidence is going to the sclerosis. However, the absence of a symptom may never have such significance as its presence. The burning hands and feet, by Stannus regarded as almost pathognomonic of pellagra [123], and occurring in 63 % of our cases may be of great aid.

Summary

The vestibular symptoms have to be localized centrally in nearly all of the cases, possibly the cochlear symptoms as well. In a certain number of cases peripheral lesions may be concomitant, but can no longer be recognized as such.

The pellagrous oto-neurological syndrome is on the whole a characteristic one, distinctly different from those in other diseases, and most resembling that of disseminated sclerosis. In both diseases the brain stem is one of the places of predilection.

CHAPTER V. AETIOLOGY

Looking back at the aetiology, the cause is obviously avitaminosis, because these patients have been observed in several camps on different dietary articles, having in common only the small quantity of protein, fat and vitamins. Quite otherwise was the position when the first scores of patients were observed. Exogenous intoxication was seriously considered in the absence of similar reports from other camps, and could only be put out of court in the course of time. Intoxication by cyanogenic foodstuffs seems still to be seriously considered in recent literature (see for instance Wright[143]). Such affections as described in this work, however, were often observed in patients who never ate cassave, maize, sugar-cane, millet, guinea corn or peas, and very rarely indeed beans (to recapitulate the enumeration given by Wright[143]). Prussic acid may play an additional role in some countries, but avitaminosis alone certainly can bring out all the symptoms.

In the literature available in the camps only the *miners' nystagmus* was reported as a form affecting larger groups of people[142, 13, 5, 17, 74]. There are some points in common (nystagmus, evoked or increased by certain head positions, eyelid nystagmus), but the differences are overwhelming. The aetiology, the frequent occurrence of oscillatory forms of nystagmus, the precipitation by upward gaze and by darkness, are as many salient points of dissimilarity[142, 13, 54, 89].

Looking at the symptom complex from the point of view of *vertigo*, there are two diseases which consistently show vertigo affecting larger groups of people, *pellagra* and *Gerlier's disease* or *paralytic vertigo*). On getting access to more literature after the war, nystagmus was moreover found described by Lewy et al. in pellagrins (the greater part being subclinical and mild cases)[70], by Kinnier Wilson in pellagra[54], Stannus in B_2 complex avitaminosis[124]

and Bicknell and Prescott in ariboflavinosis[11]. No other book from the bibliography at the end of this thesis, whether neurological, oto-neurological or otological, mentions nystagmus caused by dietary deficiency.

As to vertigo in pellagra the position is better, one will find it in every book or publication on pellagra with the initial symptoms. However, in the otological literature, pellagra as a cause for vertigo is absent again.

A. PELLAGRA

1. Introduction

A consideration of all aspects of this disease would be far beyond the scope of this book. In the preceding pages we frequently have had opportunity to touch one or another symptom of this protean disease, in its subjective as in its objective symptomatology. We will be satisfied by going only into some points of pellagra and allied deficiencies.

2. Name

The name *pellagra* is generally adopted, and in medical literature for the first time used by Frapolli of Milan in 1771[53]. However, the first clinical study on *mal de la rosa* was written in 1730 by Casal of Oviedo in Spain[53].

Probably the name originates from the Italian *pelle agra* (= rough skin), however, it may come from the Greek *pellis agra* (= affected skin), analogous to podagra. The name pellagra is midway between a name and a definition. It is too good for a name and wrong as a definition. Nobody nowadays will put malaria out of court because the air in which the disease was contracted is pure; many a physician, however, rules pellagra out, or does not think of the possibility, because the skin is not affected. In this the name has done much harm, the attention being focussed on the skin.

3. Definition

Nearly all authors agree that pellagra is a multiple deficiency disease. However, now and again the tendency is observed to

regard pellagra as a nicotinic acid deficiency. The name pellagra was given to a disease, occurring under natural conditions, and nothing is changed as to that. Food lacking nicotinic acid often will lack other factors of the B_2 or the whole B complex also. Second, in the diminished food intake and disturbed adsorption, often found in pellagra, lies another cause for a polydeficiency. Third, by administration of nicotinic acid many and important symptoms of natural pellagra can be cured, but rarely all.

The name *P.P.* (*pellagra preventive*) *factor* was given by Goldberger and Tanner in 1925 because they considered it improbable that the little amount of protein present in pellagra preventing doses of yeast was responsible for the beneficial effect. Thus they assumed another, not yet known, principle in yeast, the P.P. factor [43]. *Nicotinic acid* being isolated in 1867 by Huber [53], it is curious that only in 1937 Elvehjem et al. discovered the curative effect of nicotinic acid in *black tongue*, which was since long regarded as the *canine* analogue of human pellagra. Therefore they supposed that it would cure human pellagra as well [35]. In the same year the confirmation hereof was reported by Spies, Cooper and Blankenhorn, which was soon substantiated by the results of many others.

What I wish to make clear by this history is that Goldberger and Tanner never said that the P.P. factor had to be one pure chemical substance; but that, when Elvehjem et al. found nicotinic acid curative in black tongue, and others that it cured many conspicuous symptoms of pellagra, everybody was apt to think that the problem was solved. Gradually it dawned upon the investigators that many other symptoms remained in pellagrins after saturation with nicotinic acid, and that for the alleviation of these thiamin, riboflavin and (or) pyridoxin were necessary.

What has stuck in the mind of the average physician is the bright discovery that nicotinic acid cures pellagra, and not the deceptions that followed. Therefore we cannot take enough care to delineate pellagra as a multiple avitaminosis, and not as a nicotinic acid deficiency, which is not intended in the least to be a misappreciation of the untiring efforts of

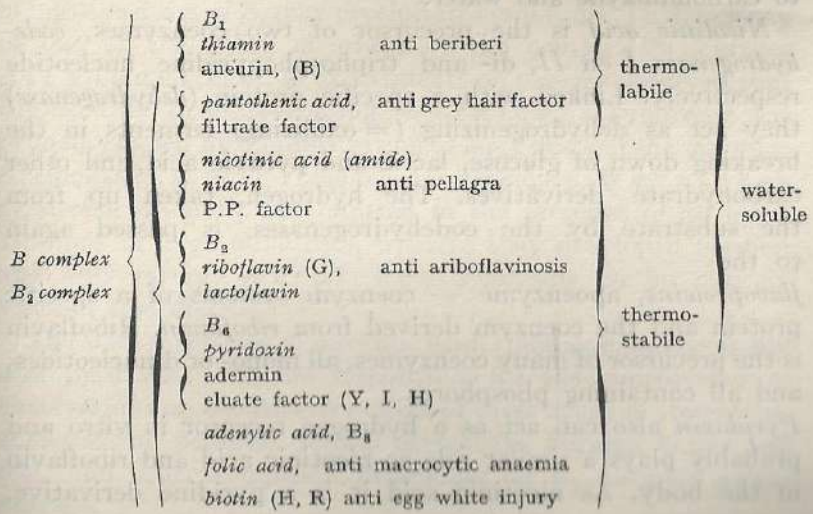
many investigators to discover which symptom in natural avitaminosis is caused by which vitamin. We have frequently had opportunity to observe the results of these efforts in the comments on the symptomatology, and the controversy between different authors. Of course there are many points of agreement, and every further step in disentangling this problem is of the utmost importance. But the association pellagra — nicotinic acid is, in a way, nearly as dangerous as that: pellagra — skin.

Tendeloo always insisted upon a definition being reversible [137], which seems a reasonable demand; what is lost in conciseness, will be gained in less misunderstanding. Therefore the following *definition* of pellagra is proposed:

A multiple deficiency disease which affects either the digestive tract, or the (central) nervous system, or the skin, or two, or all of them simultaneously.

4. The vitamin B complex

There is considerable confusion in the nomenclature of vitamins of the B complex, because historical, teleological and chemical tendencies cross each other. In addition different teams of investigators give different names and in different languages. Finally, we are in an epoch of discoveries of new vitamins.



This table does not show all the constituents of the B complex and is composed from Bicknell and Prescott[11], Eddy and Daldorff[33] and Stepp and Kühnau[128].

Bicknell and Prescott 1946[11]:

B_1, nicotinic acid, riboflavin and adenylic acid are known to play an important part in the tissue metabolism of the carbohydrates. All of them are (precursors of) *coenzymes*, i. e. they have to be linked to other enzymes, called *apoenzymes*, before they can unfold their activity. The coenzymes and their precursors have to be obtained from dietary sources, the apoenzymes are synthesized in the body.

Adenylic acid (adenosine monophosphate) is a phosphate carrier, it can take up phosphorus to the triphosphate compound and give it again to other substances. In this way it catalyzes the phosphorylation of B_1 and glucose. Glucose must be phosphorylated before being broken down.

B_1 also, before becoming an active enzyme. Thus carboxylase and cocarboxylase are formed.

Carboxylase is a enzyme — coenzyme system: protein — B_1 pyrophosphate magnesium.

Cocarboxylase is B_1 pyrophosphate. Both are required for the oxidation and decarboxylation of pyruvic acid, an intermediate derivative of glucose in its process of combustion to carbondioxyde and water.

Nicotinic acid is the precursor of two coenzymes, *codehydrogenase I* en *II*, di- and triphosphopyridine nucleotide respectively. Linked with a specific protein (*dehydrogenase*) they act as dehydrogenizing (= oxidizing) ferments in the breaking down of glucose, lactic and pyruvic acid, and other carbohydrate derivatives. The hydrogen, taken up from the substrate by the codehydrogenases, is passed again to the

flavoproteins, apoenzyme — coenzym systems of a specific protein and the coenzym derived from *riboflavin*. Riboflavin is the precursor of many coenzymes, all mono- or dinucleotides, and all containing phosphorus.

Pyridoxin also can act as a hydrogen receptor in vitro and probably plays a similar role as nicotinic acid and riboflavin in the body. As nicotinic acid it is a pyridine derivative.

Pantothenic acid and *biotin* are also suspected to be components of the same coenzyme systems[11].

Summary

We see that B_1 is acting in the decarboxylation and oxidation of pyruvic acid; nicotinic acid and riboflavin in the dehydrogenation of carbohydrates and their intermediate products, adenylic acid in the phosphorylation of glucose and vitamins.

Pyridoxin probably, and pantothenic acid and biotin perhaps play a similar role as nicotinic acid and riboflavin.

Comment

There are many intricate chemical interrelations between the coenzymes — enzymes, glucose and its intermediate products, and adenylic acid. They are only partially known and even then, often only with probability. Partly these reactions seem to have the character of chemical equilibriums, and since also the coenzymes have crosswise reactive chemical relations, all this in the future may be an explanation for the following observation of Sydenstricker. He noticed that in cases of lack of the whole B complex the administration of massive doses of B_1 may precipitate symptoms of a deficiency of one of the other members of the complex[135]. Further Alexander et al. in experiments on pigeons observed that the need for B_1 in developing Wernicke's syndrome was probably raised by administration of large doses of the vitamins A, riboflavin, C, or D. These pigeons developed Wernicke's syndrome when B_1 was omitted in the presence of all other vitamins in large quantities, whereas they developed beriberi and only rarely Wernicke's syndrome on an entirely vitamin free diet[1].

The similar activity of nicotinic acid, riboflavin and probably also pyridoxin, may be responsible for the controversy in observations on the curative effect of these drugs in stomatitis, cheilosis and perlèche, scrotal dermatitis, burning hands and feet, and other symptoms depending on B_2 complex avitaminoses.

5. Nicotinic acid

This vitamin precursor, responsible for many and important symptoms in pellagra, has the same vitamin activity as several other related drugs, among which *nicotinic acid amide* and the *diaethyl amide of nicotinic acid* (= *nikethamide* B.P., or *coramine*).

In the human body it is present as its amide, or as codehydrogenase I or II [11]. In future, when speaking of nicotinic acid, the total of codehydrogenases, nicotinic acid and its amide, equalling nicotinic acid, is meant.

Blood level

This is 0,62—0,89 mg. % according to Querido et al. Curious enough they found it not lowered either in 10 cases of pellagra [6], or in various other diseases [93], but only in 2 cases of icterus gravis [93] and in 15 out of 21 normal pregnant women [72]. The blood corpuscles, in which the greater part of the blood nicotinic acid is present, seem to cling tenaciously to this vitamin, even in pellagra. Later, Justin-Besançon and Lwoff found a low nicotinic acid blood value (0,48) in a severe case of pellagra [53]. These normal blood levels in pellagra were substantiated by investigations of Field, Melnick et al. [36] and others [94, 53]. Even on administration of nicotinic acid in healthy individuals and in pellagrins the blood levels are influenced in the same way in both groups (Melnick et al. [94, 53]).

The liver and muscles are notably depleted of nicotinic acid in pellagra, not the blood [95, 53, 11].

Urinary excretion

In the urine the following derivatives of nicotinic acid are found: nicotinic acid, its amide and nicotinuric acid (with vitamin activity), and trigonelline (without vitamin activity). However, only part of the nicotinic acid ingested is accounted for, some 70 % does not appear in the urine (Melnick et al. [94, 95]).

Trigonelline occurs also in coffee and cocoa; from the use

of these beverages it appears in the urine. Further some confirmed smokers metabolize nicotine into trigonelline, which appears in the urine (Melnick et al. [76]), possibly via nicotinic acid. It is curious that Bing in his 1945 German edition mentions that Wagner helds smoking responsible for the reduced incidence of pellagra in males [13]. Generally, however, pregnancy, childbirth and lactation are regarded as causes for the greater incidence in women.

On the whole, urinary analysis of nicotinic acid has proved unreliable as a means of diagnosing a deficiency (Querido [95]).

It was believed for some time that the urinary *coproporphyrin* level was proportional to the degree of nicotinic acid deficiency, and a colour reaction was devised to indicate this compound (Beckh et al. [9]). However, Watson et al. on the one hand could find no parallelism of this reaction to other evidence of nicotinic acid deficiency, on the other proved that the reaction was due to *urorosein*, the presence of which is not pathological [141].

In 1941 Najjar and Holt found another substance in the urine, called F_2, the amount of which in the urine parallels the degree of nicotinic acid deficiency [84]. There is no agreement as yet on the chemical structure of this compound [75, 11]. Quantitative tests can be performed with the aid of a fluophotometer [84].

Human biosynthesis

Analogous to similar experiments on thiamin and riboflavin biosynthesis [95, 11], Ellinger et al. suggest that nicotinic acid is synthesized in the human gut. Administration of sulphaguanidine or succinyl sulphathiazole caused a drop in the urinary secretion of nicotinic acid. Both are drugs of little solubility with bacteriostatic effect on the intestinal flora [34].

Querido in his two excellent reviews [94, 95] on recent advances in nicotinic acid and pellagra biochemistry, infers that this biosynthesis may be the explanation for the fact that the nicotinic acid contents of the diet often is not related to the pellagra preventing value. Since certain carbohydrates

are favourable for the intestinal biosynthesis of B_1, certain proteins or (and) aminoacids may favour nicotinic acid production. He reports Krehl's observation from Elvehjem's laboratory, that adding 40 % maize to a diet satisfactory for rats brings about retardation of growth, which can be abolished again by ingestion of 1 mg. nicotinic acid per 100 g. food. Tryptophane has the same effect, in doses 50 times those of nicotinic acid. Casein does the same qualitatively. They conclude that extensive changes in the intestinal flora may play a role. Certain is that the protein contents of the food has a great influence on the nicotinic acid requirements. Woolley discovered in addition a substance in maize which raises the nicotinic acid requirement, and was able to concentrate this substance [95]. Probably this is indole-3-acetic acid (Kodicek et al. [64]). With these recent findings the old theories of aminoacids, proteins and maize have regained their proper place.

Apart from the influence sulpha drugs may have through bacteriostasis in the gut, there is another, limited to those with a pyridine ring. It is believed that bacterial enzyme systems take up the sulphapyridine compounds, thus blocking access to nicotinic acid which also has a pyridine ring. In this way reproduction of the bacteria is said to be interfered with [11].

All sulpha drugs may impede bacterial synthesis of B_1, riboflavin and nicotinic acid; those with a pyridine ring in addition may prevent human enzyme systems from taking up the chemically related nicotinic acid and pyridoxin. The former fact is a reason to supply multivitamin mixtures with sulpha drug therapy, of which favourable effect on the toxic symptoms is reported [11].

Especially dangerous in this respect is the mistaking of pellagrous diarrhea for bacillary dysentery and subsequent administration of a sulpha drug.

Summary

1. Most diseases do not show a drop in the nicotinic acid blood level. Among these, curiously, is pellagra. The liver and muscles are drained, not the blood.

2. The only reliable laboratory test on nicotinic acid deficiency may be in the future Najjar and Holt's F_8 test.

3. The human need for nicotinic acid, riboflavin and B_1 is not only influenced by the dietary supply, but also by intestinal biosynthesis. This in turn is dependent upon the chemical condition of the intestinal contents. Tryptophane and casein may be given instead of nicotinic acid, probably because of this bacterial synthesis.

4. Sulpha drugs diminish intestinal production of B_1, riboflavin and nicotinic acid; and a substance in maize impedes the biosynthesis of nicotinic acid and pyridoxin.

5. Sulphapyridine drugs may prevent human enzym systems from taking up nicotinic acid and pyridoxin.

6. The administration of sulpha drugs should be supplemented by multivitamin treatment.

6. Pathology of the nervous system

Publications are rather scarce. Singer and Pollock [114] described their observations in 14 cases:

Vessels: in the pia and in the brain and cord there is proliferation of the walls and perivascular exudate, both in slight degree. In the exudate lymphocytes are present. Degenerative changes are found in the vascular walls. In the brain and cord there is in addition thickening of all coats. The lumen is usually somewhat widened, in 3 cases haemorrhages are found, twice in the cord and once in the midbrain.

Neuroglia is increased, especially in the outermost layers of the brain cortex.

Nerve cell degeneration is marked in the cortical cells (notably of the central and paracentral convolutions), the hippocampus, the cerebellar dentate nucleus, the central ganglia and the *nuclei of the cranial nerves*, Clarke's column, the central gray matter of the spinal cord (notably in the posterior horns), the posterior root ganglia, the sympathetic and Auerbach's and Meissner's plexus in the intestine. These degenerative changes are predominantly axonal (with secondary cell reaction), but there is also direct cell degeneration. The pathologic picture is considered identical with that of

Meyer's central neuritis [77]. Fibre degeneration is found in the radial cortex fibres and in the spinal cord, notably in the posterior columns. The anterior and posterior roots show a few degenerated fibres. Except in the 3 cases of haemorrhages there were no particulars in the brain or cord substance macroscopically. In none of the cases the abovementioned findings were as marked as they may (partially) be in dementia senilis, general paralysis and cerebral syphilis [114].

On the whole there are wide spread lesions, with little exudation, somewhat more proliferation and very marked degeneration. There are all three the qualities which Tendeloo demands to make the histopathological diagnosis of inflammation then. According to Tendeloo we should call it a *degenerative inflammation* [137].

Scott, in his outbreak of *central neuritis* in people harvesting on the cane fields, who in this time feed exclusively on the cane crop, was able to perform two post mortems. He notes remarkable points of resemblance with Singer and Pollock's cases and consequently with Meyer's central neuritis, thence he adopts Meyer's name, whereas the disease in Jamaica was always called peripheral neuritis. He finds little Wallerian degeneration in the peripheral nerves; marked degeneration in the central nervous system, in the axons more than in the cells. We will not give a summary of all his findings, but relate a few points only. In the pons there is a marked degeneration of white matter and of the cells of the principal and descending vestibular nucleus. The fillet (lemniscus, probably both medial and lateral) is considerably involved. The auditory nerve shows little marked degeneration "of the majority of its fibres, while the grey matter shows fatty changes in the large nerve cells, but not marked." In the optic nerve there is wide spread degeneration along practically all the fibres. No nystagmus, vertigo or deafness were entered in the case reports of these two patients, though deafness and the absence of nystagmus was recorded in some others not terminating fatally [107].

The results of Singer and Pollock are substantiated by other investigators [74, 33]. Chotzen also noted haemorrhages in the midbrain of some pellagrins [22].

Comment

On the subject of Scott's central neuritis the reader is requested to reread the comment on neurological examination. Probably this has been an acute outbreak of B complex avitaminosis by the establishment of pure carbohydrate diet (cane) and heavy work (harvest) in people who are already more or less deficient in B vitamins and animal protein, and eat maize in addition. We know at this time that increase of carbohydrate at the cost of protein increases the requirement of nicotinic acid (Krehl [95]). If, in the last sentence, we substitute fat for protein, we may substitute B_1 for nicotinic acid [11, 33, 128]. The increased requirement of vitamins specially concerned in carbohydrate metabolism by physical exertion is observed by many investigators and generally accepted.

The changes found by Singer and Pollock and by Scott include degeneration in the vestibular nuclei and white matter in the pons, further Scott found less marked degeneration in the auditory nerve. These findings are considered to be the underlying pathology also of our nystagmus, vertigo and hearing loss cases.

7. Symptomatology

Pellagra is a protean disease which has the same potential polymorphology as syphilis, and the same treacherousness as some forms of malaria.

We will review the symptomatology in our patients with regard to pellagra, including the symptoms more generally held to be due to ariboflavinosis.

a. The *vertigo* is a common initial symptom, often not marked. Castellani and Chalmers write: "Of all the nervous symptoms early exhibited, the vertigo is the most common, and should be carefully inquired for, as the patient often does not associate slight morning vertigo with the disease, and will therefore omit to mention the fact" [20].

b. The same applies to *burning hands and feet* in a patient who complains of *stomatitis*. Both are common in pellagra.

c. Symptoms from any part of the *digestive tract*, perhaps most constantly *gastritis*, are common in early pellagra.

d. *A-* or *hypochlorhydria* is consistent.

e. *Eyes*: *Amblyopia, diplopia, mydriasis, photophobia* and *lacrimation* are early symptoms [74]. The *staring, lifeless gaze* is characteristic.

f. Slight *psychic disturbances,* commonly mistaken for neurasthenia, are often present, *sleeplesness* and *headaches* also.

g. *Loss of balance, rombergism* (often *backwards*), *ataxia* and *exaggerated reflexes* are common in the initial stages.

All these symptoms are to be found with Manson Bahr [74], Niles [85], Castellani and Chalmers [20], Vedder [140], Bing [13], Wechsler [142], Kinnier Wilson [54], Justin-Besançon [53], Bicknell and Prescott [11], Eddy and Dalldorf [33], and others; in addition in many publications of the bibliography at the end.

We come now to some more rarely described symptoms.

h. *Nystagmus,* described by Stannus in B complex avitaminosis [124], by Kinnier Wilson [54] and Lewy et al. [70] in pellagra. *Mydriasis, anisocoria* and *deformity* of the pupils were described in pellagra by Lewy et al. [70].

i. *Deafness* (see under symptomatology) is common.

j. There is the *scrotal dermatitis,* an initial symptom (Goldberger's Rankin Prison Farm experiment [42], and others [33]).

Finally, other symptoms frequently occurring in this oto-neurological group were observed, such as *weakness of lateral gaze* and of *convergence,* Bing's *ocular cogwheel sign* and some peculiar, more rarely occurring symptoms. The oto-neurological symptoms are considered to fit in a central nervous system affection caused by pellagra and associated deficiencies (nicotinic acid, riboflavin, B_1 and perhaps pyridoxin). Singer and Pollock described the underlying pathology in the central nervous system [114]. The evidence of pellagra being the cause is circumstantial, but strong in my opinion. Unfortunately we were not in a position to bring the proof by administration of large quantities of vitamins.

All the symptoms enumerated under a—g are described as initial ones in the books referred to, occurring before the dermatitis appears. The same is true of the others, at least that they may appear before the characteristic dermatitis. This depends largely on the opportunity the sun has to elicit

the typical dermal reaction. As said before, the patient as a rule will only come into the sunshine when forced to do so.

The disease runs a course with seasonal and spontaneous remissions, but will relapse with deadly certainty, if dietary conditions are not considerably improved. This is true of all symptoms, and may confuse the clinical picture. One part of the digestive tract may be chiefly affected in one exacerbation, another in a following one.

The disease is not necessarily bound to develop to more serious stages. Manson Bahr mentions that these initial symptoms may recur for years and years without the appearance of dermal signs. In some the gastrointestinal symptoms predominate, in others the nervous, in others again the cutaneous [74].

For the description of the full-blown disease and the end stages I must refer to the standard textbooks. A few remarks: Manson Bahr: Mental symptoms supervene in $\frac{1}{8}$ or $\frac{1}{4}$ of all cases [74] (probably the more serious ones are meant, psychoses, delirium and dementia). The dermatitis is not necessary for the diagnosis, also in the later stages.

8. Diagnosis in early cases

One symptom, of course, will not make the diagnosis, but when we find two or three, or even four, a tentative diagnosis may be made and put on the test by the therapy. *Conditio sine qua non* for making the diagnosis at an early stage, however, is that the possibilities are known and inquired or tested for. Further that pellagra is not ruled out because of the absence of dermal lesions (in which mostly scrotal dermatitis is not asked or looked for). The standard textbooks state these facts, but apparently do not emphasize them enough, except Justin-Besançon, whose book is little known to the general physician. He states: *"Trop de médecins se figurent encore que la pellagre consiste en un érythème chez un mangeur de maïs, tout comme le scorbut est réalisé par des hémorragies buccales chez un marin et le béribéri par une polynévrite oedémateuse chez un Chinois"* [53].

Exaggerated, but with a good intention. Those acquainted with the initial and monosymptomatic forms of pellagra, are often amazed to learn another's diagnosis. Probably Justin-Besançon also experienced this. "*L'érythème pellagreux est très charactéristique. Malheureusement, c'est le moins constant et le plus transitoire des symptômes de la pellagre (dans des pays peu ensoleillés)*". And: "*L'opinion de* Bouchard (1862) *toujours d'actualité: Chaque année, des pellagreux viennent en grand nombre dans les hôpitaux; mais l'attention n'est pas éveillée dans ce sens, le diagnostic basé sur le symptôme dominant suffit à l'observateur; rarement la vérité se découvre*" [53].

Pellagra is called *malo del sol, scotatura di sole, malattia della insolazione di primavera.* Strambio held malnutrition responsible and described sunlight as revealing an inapparent disease [53]. A remarkably clear insight as early as 1786. Further he noticed that the pellagrin stays in the shadow, thus avoiding dermatitis, but not pellagra [53].

Why insist then upon a dermatitis? Pellagra is known to affect the digestive tract, the nervous system and the skin. Theoretically speaking it is absurd to expect that the skin, the least specialized and vulnerable of the three, will initiate the picture. In practice also pellagra may well and should be recognized before the skin lesions appear.

The well-known triad: dermatitis, diarrhea and delirium or dementia is more dangerous still than the association pellagra-skin. A third and even a second d may well be that of death. In these cases it is mostly the dermatitis that first falls out of the triad.

I saw the following happen: A man has bouts of diarrhea and stomatitis, vertigo and burning hands and feet. Pellagra is diagnosed. "No", says another, "this is chronic bacillary dysentery". On half an hour exposure to sunlight dermatitis. "Well, he is not demented."

Used in this way, the d triad may be disastrous. It was not in this case because vitamins were not available. The 3 d's, under the mentioned restrictions, are useful to remember that lesions of the (central) nervous system, digestive tract and skin may occur.

Pellagra is rarely so kind (to the physician) as to show affection of all three of its domains. At least when compared

with the infinitely greater number of patients who show only part of the syndrome.

The history should include the patients' dietary, in which we must remember that the nicotinic acid requirement is increased in lack of (animal) protein (Querido, Krehl [94, 95], Monteiro et al. [79] and many others). Alcoholism is a frequent cause for B_1 and B_2 complex avitaminosis and should be inquired for.

Possibly Najjar and Holt's F_2 test will be useful. When due suspicion has arisen, a test with vitamins of the B complex is indicated (see therapy), and the tentative diagnosis may be substantiated by the results.

Summary

Inquire, look and test for symptoms of the digestive tract, the nervous system, and the skin. Lesions of the skin are characteristic, but often absent, and in that case immaterial.

In the history the diet, alcoholism and exposure to sunlight are important.

Perform the F_2 test in the urine.

Test a tentative diagnosis *ex juvantibus.*

9. Pathogenesis

A feature observed in many affected structures is abnormality in the width of the blood vessels. We see this in the mucous membrane of the digestive tract, in the skin, in the retina, and post mortem in the brain and pial vessels as well. There may be hyperaemia or anaemia in irregular patches in the digestive tract macroscopically and microscopically (see also cases of Ceelen [21], Herzenberg [50], Denton [29], and others). In early cases the mucosa is diffusely hyperaemic. More or less the same is observed in the retina (Mohr [78], Schwartz [106]). Smitskamp observed predominantly narrow capillaries in the fingers and toes (to be published). In the irritative character the oto-neurological vestibular symptoms show on the whole, it is tempting to assume hyperaemia in the brain stem as the cause, in later stages probably

more inclining to anaemia (see comment on hyperexcitability).

The hyperaemia may be part of the inflammation found microscopically in the brain as in the affected parts of the digestive tract, nervous system and skin. However, in the fingers and toes it gives more the impression that the disturbance is exclusively vascular. In the wide spread lesions of the sympathetic nervous system it is quite possible that these are at the root of the latter vascular abnormalities. Lesion of the sympathetic centre in the hypothalamus is quite possible in the extensive lesions of the central nervous system. I did not find anything in the literature as to this.

We saw that nicotinic acid and some allied vitamins play an important role in carbohydrate metabolism. Many investigators suspect intermediate products of carbohydrate metabolism to be the toxic agent, causing the lesions.

Quite another and interesting point of view is taken by Petri, Norgaard and Bandier. They found that:

Dog and pig pellagra produced by gastrectomy does not respond to yeast or nicotinic acid, but immediately so, if human gastric juice or ventriculin M.C.O. (dried pig's stomach) is given in addition. Similar observations were made in certain cases of human pellagra. The authors conclude that the stomach has a "particular anti pellagrous function", which function may be decreased in varying degree in pellagra. In totally gastrectomized pigs nicotinic acid had no curative effect; it had in pellagra induced by partial gastrectomy [91].

These experiments are too ably carried out and judged to be dismissed without further comment. A gastrogenic influence is not at all incompatible with the other theories on the pathogenesis of pellagra. Further their findings seem to be substantiated by a recent publication of the Gillmans, who in pellagra in children find that ventriculin is life saving, whereas vitamins are not [41]. Strange is, that from their table a deleterious effect of vitamins, whether given alone or with ventriculin, must be inferred.

However, the observations of Petri et al. on the one hand, and of Gillman et al. on the other, are to be borne in mind when a pellagrin does not readily respond to multi-

vitamin treatment. The "irreversibility" of a pellagrous process might be reversed by the introduction of ventriculin in vitamin resistent cases.

10. Importance for countries where full-blown pellagra is not endemic

Initial pellagra need not develop to a well-established syndrome [74]. Patients may begin with any symptom of those enumerated above as occurring in the initial stage. One will begin with vertigo, another with stomatitis, a third with diarrhea. Since it is beyond any doubt that vertigo, nystagmus, tinnitus, deafness and inflammation of any part of the digestive tract may be caused by avitaminosis of one or more members of the B group, it is wise for the oto-rhino-laryngologist to contemplate deficiency as a cause in any patient with "idiopathic" affection of one of the abovementioned structures. Especially so at a time following a period of malnutrition and in which the use of animal protein is still not yet equalling that before the war, as is the case in Holland.

"Idiopathic" Ménière's syndrome, when of central origin, should be suspected to be caused by avitaminosis. Curious is that in 1946 Van Deinse of Amsterdam in an extensive oto-neurological examination of 63 cases showing Ménière's syndrome, finds 50 to be "idiopathic". Of these 50, 47 show a central disease picture; and vasomotor disturbances are considered to play an important role [27]. Valkenburg in 1942 describes an "epidemic" of Ménière's syndrome in Holland [139]. Of 28 patients 23 show vestibular disturbances without such of the cochlear system. Some case reports are given, in which more positive central symptoms are to be found, such as vestibular dysharmony. From an ear, nose and throat specialist in Holland I hear that so many patients with vertigo report these years; from a neurologist that many people with burning hands and feet report, to whom he gives vitamin treatment. I dare not judge whether the large number of central lesions in Van Deinse's investigation as compared with earlier observations in Ménière's syndrome is due to a more extensive and

expert examination or to a real increase in centrally localized lesions. The latter is more probable in my opinion.

By including avitaminosis as a cause for vertigo, deafness or tinnitus we possibly will be able to diminish considerably the number of "idiopathic" cases. This reasoning applies especially to countries with little sunshine, with a small chance for pellagra to be "revealed".

Harris and Moore were, so far I know, the first who regarded Ménière's syndrome from this point of view in 1940, led hereto by the frequent occurrence of vertigo in pellagrins. They treated 20 cases with 250 mg. of nicotinic acid and 20 mg. of B_1 per day; 17 were entirely cured. However, it is pointed out that complete relief may require several months [48]. Selfridge started the same in perception deafness in 1939 [111]; Atkinson uses nicotinic acid as vasodilating drug in a part of his Ménière cases [3].

11. Comment on deficiency Ménière's syndrome

This syndrome in pellagrins is often incomplete, in that the cochlear disturbances are not infreqently absent. The vertigo is rarely very marked and limited to clearly cut attacks. As such these are symptoms speaking for central rather than for peripheral origin.

Strange is the absolute absence of pellagra as a possible cause for Ménière's syndrome, perception deafness and tinnitus in oto (-neuro) -rhino -laryngological textbooks. On the whole it is curious, that nystagmus is reported only in 1940 in pellagra (Lewy et al. [70], Kinnier Wilson [54]), and this whilst in the Southern States of the U.S.A. are some hundred thousands of pellagrins with some thousands of deaths annually. Another point of this oto-neurological syndrome is that it is infrequently detected. It dawned upon me some 6 months after the beginning of the symptoms, when stomatitis, scrotal dermatitis, retrobulbar neuritis and also vertigo were in full swing. At this time Bruining, in a neighbouring camp, had not yet noticed vestibular disturbances, but had observed those of the cochlear system. Kuilman, more than a year later, when hearing of these patients

from Bruining, was sceptical, because he never consciously saw one. After being shown some specimens, he observed a very large number, some 500, in little more than a year [66,65]. There were other camps in which deafness, vertigo and nystagmus were not noticed. In the initial as in the later stages of pellagra there are many other, more annoying and life threatening symptoms, which may mask these rather inconspicuous ones. An occasional severe dizzy spell is diagnosed as a "case of Ménière". When referred to a specialist this one looks at it from an otological standpoint and fails to notice any relation with deficiency, unless suspicion is aroused by a conspicuously large number of cases and when disturbances of the VIIIth nerve system are more or less awaited.

B. GERLIER'S DISEASE

This little known malady, also showing vertigo affecting larger groups of persons, was dismissed in Bandoeng and Batavia, because we never saw anything resembling it there. Because of some observations in Pakan Baroe, however, this disease will be discussed.

Literature is scarce, for reasons becoming obvious on learning the particulars. Bing [13] and Wechsler [142] describe it; there are a few lines in the "Handbuch der Neurologie" (Bumke und Förster), and some publications among which I could read that of Couchoud [23] (1914) and of Roch [102] (1932), and obtain that of Rehsteiner (1925)*. In Rehsteiner's elaborate publication one will find a review of the literature on the subject [100], as in Couchoud's [23].

1. Time and place of occurrence

Gerlier observed the disease for the first time in 1884 near Geneva, notwithstanding being for 20 years a practising physician there, and proposed the name *vertige ptosique*. Later

*) Dr. Rehsteiner of St. Gallen (Switzerland) sent me a reprint by the kind intermediation of Prof. Dr Roch, Geneva.

he suggested the name *vertige paralysant*. David, also near Geneva, observed the same disease, independent of Gerlier, in the same year. Curiously enough, also in 1884, the Japanese physician Nakano discovered a disease, endemic in Northern Japan, and existing since a long time, called *kubisagari* by the inhabitants, which means: "Those who cannot keep the head up". Miura in 1896 pointed out that the disease was identical with that of Gerlier and David. On reading Gerlier's first publication, other physicians remembered to have witnessed similar „epidemics" in other parts of Switzerland, in 1874 and 1881. Later the disease was also observed on an island of Southern Japan.

The disease practically disappeared in Switserland after 1900. Rehsteiner observed a small "epidemic" of 7 cases, of which he examined 5, in 1924[100]. Roch described an isolated case in 1932 and states that this is perhaps the last case of "Gerlier" in Switzerland[102]. Rehsteiner, however, in a personal communication, tells me that he thinks it not at all impossible that more cases occur, but that the diagnosis is missed because the clinical picture is so little known.

In Japan the disease is till prevailing, so far I know.

The abovementioned facts are obtained from Couchoud[23], Rehsteiner[100], and Roch[102].

We see that the disease was noticed and described in Switzerland and in Japan in 1884, though it occurred before, giving the impression that at a certain time the human mind becomes ripe to associate certain observations and arrive at a conclusion. Gerlier called it *vertige ptosique*, or *vertige paralysant*, the Japanese *kubisagari*, each name expressing some characteristic features of the disease.

2. Symptomatology

Mostly young, robust individuals are affected, generally in groups or families, and exclusively when they *work in or around stables*. When this trade is abandoned, the disease disappears. Only Couchoud reports one case in which a relapse occurred 9 years after the patient had contact with stables. In Switzerland cows, in Japan horses are incriminated[23].

The disease comes on in attacks in which vertigo is but one and often a minor symptom. The *attacks* consist of *palsies*; in order of incidence as follows:

Ptosis, muscles of the back of the neck, extensors of the limbs, muscles of mastication, and more rarely those of the *face, pharynx, larynx* or of the *back*.

Vertigo and *blurred vision* accompany or precede the palsies. The vertigo may be severe or slight, there is neither nausea, nor cochlear disturbance. *Diplopia* and *amblyopia* occur not infrequently. Miura found in some cases hyperaemia of the optic discs in the attack. Others noticed similar symptoms in the interval, but infrequently[100, 23].

Pains in the back of the neck and body are inconsistent, but sometimes severe. Between the attacks there is slight ptosis and *weakness of convergence*, at most.

The attacks do not last longer than 10 minutes on the whole, but may succeeed one another very rapidly, with incomplete remissions, so that the whole may give the impression of lasting several days. In other cases there are solitary attacks of light degree, hardly incapacitating the patient. In these light attacks ptosis is always, and sometimes the only symptom present.

Bodily exertion favours precipitation of the attacks, rest makes them subside. The tired muscles especially are liable to be affected. The disease occurs *in warm summer months only*; attacks in wintertime are observed, but are extremely rare.

The course is *benign*, remaining disability or death never occurred.

Rehsteiner saw in 5 cases (in the interval) no nystagmus, though this was especially tested for[100].

3. Own observations

It was rather extraordinary that on a certain day in 1945 in Pakan Baroe two men who were nephews, entered my policlinic room, both with an attack of Gerlier.

They lived side by side, were young and strong Eurasian boys, working on the railroad and known to have weakness

of convergence, first degree bilateral horizontal nystagmus, slight perception deafness and little marked attacks of vertigo. They had just finished a long day of heavy manual work and both, to their great astonishment, developed an attack of ptosis, weakness of the muscles of the back of the neck and extreme fatigue in chewing their food. They knitted the brow in a futile effort to raise the upper eyelids; the head came into clonic nodding movement by the effort to keep it up (kubisagari!). This attack soon passed away, but they had more, always when tired from heavy work.

One other patient was observed in Pakan Baroe with attacks of ptosis only; he had in addition a peroneal palsy in one leg, which lasted for months. He showed no nystagmus.

Unfortunately no written records on these 3 cases are available. In Bandoeng one patient (no. 132) was observed who showed slight ptosis.

None of the patients worked in stables, or with cows or horses.

On reading the manuscript two friends of mine were highly interested, one having seen about 10 more of these cases and the other about 20 in an "epidemic" in Pakan Baroe camps. Some of these were diagnosed first as imitative hysteria and later as rheumatism, because of the accompanying pains and because massage helped them (see Roch [102]).

4. Aetiology

Gerlier suggested an infectious cause in the cow's dung, but was unable to prove this; neither has any observer in Europe been able to isolate a microorganism.

Couchoud, in Japan, cultured small gramnegative cocci from the cerebrospinal fluid and milk of two patients with kubisagari. On subcutaneous injection of the cultures cats developed transient multiple palsies in 3—12 hours, closely resembling Gerlier's disease. The attacks ceased in a few days, the animals being quite well again. From the cerebrospinal fluid of these cats the microorganism could be cultured again, and used to infect other animals. The organism was called *micrococcus paralysans*; it was agglutinated by a 1 : 25 dilution of serum of other kubisagari cases. After the

two mentioned cases Couchoud no longer succeeded to obtain the germ from other patients. In Japan a spontaneous similar disease was occasionally observed in horses and cows; Gerlier observed it in cats and fowl. Rehsteiner tried to contaminate rabbits with serum of Gerlier cases without result. No investigator other than Couchoud has been able to isolate a germ, so that the aetiology is taken to be obscure. Direct contagiousness was denied even by Gerlier; who assumed an infectious cause in the cow's dung. He never observed direct transfer from one person to another. However, in Japan infants nursed by mothers suffering from kubisagari, contracted the disease nearly always [23, 100].

Some observers believe epidemic encephalitis to be the cause [100, 102]. A leucocytosis at the time of the attacks proves in favour of an infectious aetiology, and also in the follow up a blood picture resembling that of most infectious diseases [100].

5. Comment

The Pakan Baroe cases undoubtedly showed a syndrome, closely resembling that of Gerlier's disease. The occurrence in "epidemics" after exertion, in short lasting attacks affecting the characteristic groups of muscles, the benignity, is all the same as in Gerlier's cases. However, there was no contact with cattle. There was contact with Japanese soldiers, but nobody ever observed direct transfer from a patient to a healthy person; still less is this to be expected by an intermediate healthy person, or carrier of the germ.

Avitaminosis was a common feature of all Pakan Baroe cases. The two I observed (dismissing the cases with only ptosis) showed the oto-neurological syndrome caused by nervous pellagra.

Gerlier's disease certainly must be an encephalitis in which the brain stem and optic nerves are involved (blurred vision and sometimes hyperaemic discs). Ptosis is consistently present. In more severe cases there is extension to some pathways in the pyramidal tracts or to the cord (neck and limbs).

I do not know the dietary conditions in the endemic areas

of Switzerland and Japan; from a personal communication of Rehsteiner I gather that the food in Gerlier areas is good, and the same as that of thousands of other Swiss peasants, not showing either this syndrome or pellagra. Infants nursed by mothers with kubisagari and contracting the disease, may do so because of a dietary deficiency of the mother.

I do not know whether pellagra is endemic in the kubisagari areas, but so far I know there was never any report of Gerlier's disease picture from countries where pellagra is common. Pellagra has a predilection for the central nervous system and ptosis is common in the disease [74].

6. Conclusion

Gerlier's disease was observed in Switzerland from 1874 to 1924. It is not certain that it did not occur before and after this period. Under the name kubisagari it still prevails in Japan. There are no reports from other countries. Swiss and Japanese cases have in common that they occur exclusively in people having close contact with cows, horses, or their stables.

In 1945 in Pakan Baroe ± 30 cases were seen without the mentioned contact, but who had in common avitaminosis of the whole B complex. In the affection of the central nervous system we must suspect lack of nicotinic acid and riboflavin more than of the other members of the complex.

From Japan the occurrence of pellagra is reported, from Switzerland only isolated cases [53]. For the time being we must be satisfied with the conclusion that pellagra may, rarely, produce a syndrome closely resembling Gerlier's disease.

CHAPTER VI. THERAPY

A. Own observations

Only the effect of therapy on the oto-neurological syndrome will be discussed.

On our own therapy we can be brief, owing to the fact that high grade protein and vitamins were not available or only in very small quantities. Even rice polishings were only temporarily supplied and then in insufficient amount.

In the first cases NH_4Cl was used, in doses of 3 g. a day, according to Fürstenberg et al [40]. Food without NaCl could not be prepared. This therapy had no evident results, as was to be expected in the absence of affection of the labyrinths, and was abandoned.

Tonsillectomy was performed on a few patients with chronic tonsillitis, following the line of thought of Hallpike ans Cairns [47]. This had no evident results, which was quite conceivable, on account of the central localization of the affection in question.

A little more protein (3 eggs, a slice of bloodsausage, meat ± 30 g. a day), and rest, notably of the eyes, had a benificial effect in some of the patients, objectively and subjectively. In the improved cases, however, relapses were common. Bakers' yeast 20—30 g. (wet) daily did the same. The longest period we were able to give this to a patient was 3 weeks.

Some cases treated with thiamin 5000 I.U. 3 injections weekly showed improvement, but no cure, others showed no response.

Three patients were treated with all the diaethyl nicotinamide that was left, 1 cc. per day 7 ×, subcutaneously. There were no evident results. This therapy, however, could not be continued long enough.

Schwartz saw good (transitory ?) results from fever therapy in retrobulbar neuritis cases, with administration of extra protein, in the form of 3 eggs a day. The fever was elicited by intravenous injection of typhoid vaccin. I tried this therapy on two early nystagmus cases, with adverse results, so this was stopped.

B. General principles

Pellagra is a multiple deficiency disease [140, 11], chiefly of niacin, but to a greater or less extent of many of the fractions of the B complex [140]. We must bear this in mind in the therapy of pellagrins; likewise Sydenstricker's [135] and Alexander's [1] observations mentioned under the comment on the vitamin B complex. Further we should remember Petri's [91] and Gillman's [41] observations, described in the pathogenesis of pellagra.

Therefore we must attack pellagra not only with nicotinic acid, but with thiamin [120, 70], riboflavin [120], pyridoxin [121] and in the case of macrocytic anaemia with folic acid [117] in addition [140, 11, 33, 74], etc.

With these facts in mind we can best give *crude liver extracts* in doses of 5 cc. parenterally, or 3 times a tablespoonful, both daily. In more severe cases we can add:

nicotinic acid 300—500 m.g. per day, for example 1 × 50 intravenously and 5 × 50 m.g. by mouth. Nicotinic acid has a strong temporary vasodilating effect; if this is not desired, *nicotinamide* must be given.

thiamin 10—50 m.g. daily by injection or by mouth.

riboflavin 5—15 m.g. per day by injection or by mouth.

pyridoxin 50 m.g. per day by injection or by mouth.

The more severe the case and the diarrhea, the more important is parenteral administration, on the whole.

Yeast (brewers' or bakers') contains all components, 30—100 g. daily. This must be watched, however, for untoward effects in the case of diarrhea.

In severe cases with dehydration an *intravenous saline glucose drip* containing vitamins may be applied.

All this has to be supported by a *diet of high caloric value* (2500—4000 calories) with *plenty of red meat, liver, eggs, milk, fresh vegetables, yeast* and *meat extracts*. The tragedy of the pellagrin commonly is that he is so poor that he develops the disease, is then treated, but drops back to his poor man's diet again. In America they are encouraged to cultivate small gardens, chickens or a cow. Further there are plans to mix nicotinic acid in the cornmeal of endemic areas. Spies recommends a mixture of dried brewers' yeast 25 %, peanut butter 67 % and peanut oil 8 %, in daily doses of 2 ounces (some 60 g.) which is inexpensive in America, quite palatable, and will prevent pellagra and beriberi.

In judging the effect of the therapy the spontaneous remissions of this disease should not be forgotten. On the other hand, when the therapy is stopped after apparent cure, and the patients return to their former dietary regimen, relapses are sure to occur.

The dermal and gastrointestinal lesions disappear within 14 days on vitamin therapy in cases not too far advanced; the symptoms from the nervous system, however, take much longer to resolve. The acute mental disturbances form an exception and respond miraculously to nicotinic acid [51, 74, 140, 11, 33].

In rice producing countries the rice polishings are a cheap and valuable source of B_1, nicotinic acid and riboflavin, probably also of other members of the B complex. Van Swelm in the Pakan Baroe camp made watery extracts like this:

1 volume part polishings is mixed with 4 parts water, after ½ hour stirred again. The mixture is allowed to stand for 2 hours, after which the macerate is syphoned off, boiled briefly, and given in doses of 300—500 cc. daily. This dose is adequate to prevent pellagra and beriberi. If one takes the polishings as a powder, considerable amounts of fat and protein are provided in addition. In the Netherlands East Indies many dishes were devised, in which rice polishings formed the principal constituent.

SUMMARY

In allied prisoners of war in the Far East many deficiency symptoms were observed from 1942—1945. The diet was inadequate chiefly in vitamins of the B complex, animal proteins and fat, later in caloric value as well. Among many other symptoms an oto-neurological syndrome was observed which was given the greatest attention. A group of 160 patients, exhibiting this syndrome, showed the following distribution of the constituting symptoms:

Vestibular hyperexcitability for cold water	74 %
Vertigo	63 %
Spontaneous abnormalities in the walking, pointing, or (and) Romberg test	61 %
Nystagmus (the greater part bilateral horizontal)	59 %
Weakness of lateral gaze	56 %
Headache	47 %
Weakness of convergence	44 %
Hearing loss of perceptive type, due to deficiency	26 %
Reactive vestibular dysharmony or dissociation	23 %
Anisocoria	19 %
Eagleton's symptom	16 %
Mydriasis	frequently
Bing's ocular cogwheel sign	frequently
Tinnitus due to deficiency	14 %
Ataxia of convergence movements	6 cases
Abnormality in the form of the pupils	a few cases
Positional nystagmus	a few cases
Hertwig-Magendie's deviation	2 cases
Pick's visions	2 cases

There were many other concomitant symptoms either in history or still present on examination, distributed as follows:

Hypo- or achlorhydria	very many cases
Burning and pains in hands and feet	63 %
Diarrhea, in exacerbations and remissions	42 %
Retrobulbar neuritis	31 %
Perlèche and (or) cheilosis	24 %
Scrotal dermatitis	23 %
Narrow capillaries of fingers and toes	19 %
Ataxia	16 %
Stomatitis, glossitis and (or) pharyngitis	14 %

The underlying pathology of the oto-neurological disturbances is a degenerative brain stem encephalitis. In some cases the nystagmus is elicited by lesions in the vestibular nuclear area, in other cases by disturbance in the posterior longitudinal bundle or a higher section of the fronto-ocular pathway.

There were only two cases of typical pellagra dermatitis at that time, but all these patients were observed in the second year of captivity. Later, under worse conditions and with more outdoor work in the sun, many more developed this. One died showing a well established Korsakoff syndrome.

The condition is believed to be due to pellagra, in which vertigo and many other of the enumerated symptoms are initial signs, occurring long before a dermatitis may appear. Pellagra in the sense of the disease as it spontaneously occurs, as a multiple deficiency, in which lack of nicotinic acid plays a principal role and certainly elicits many conspicuous and important symptoms, but in which disease picture lack of other members of the B complex is contributing its share.

Thus it is quite possible that a riboflavin deficiency plays the most important role in bringing out the central nervous system symptoms, the retrobulbar neuritis and some other correlating symptoms. There are observations from other investigators which seem to favour this opinion. However, in the therapy we should play safe and certainly do no harm by giving all factors of the B complex. Occasionally the addition of ventriculin should be considered.

It is imperative to remember in temperate climates that patients showing Ménière's syndrome may have early, and sometimes monosymptomatic, pellagra. In "idiopathic" vertigo cases, notably when of central origin, a search for further initial symptoms of the disease is necessary, and multivitamin B treatment should be tried or at least seriously considered. Possibly the true aetiology may be recognized also from the characteristic oto-neurological disease picture.

The same aetiology should be considered for perlèche, cheilosis, glossitis, stomatitis, pharyngitis, etc., and for perception deafness and tinnitus, in case no obvious cause is found.

SAMENVATTING

Vele deficientie symptomen werden waargenomen bij gealliëerde krijgsgevangenen in het Verre Oosten gedurende de jaren 1942 tot en met 1945. De voeding was zeer arm aan vitaminen van het B complex, dierlijke eiwitten en vetten, terwijl in de latere stadia ook de calorische waarde onvoldoende was. Naast vele andere verschijnselen werd een oto-neurologisch syndroom waargenomen, dat de meeste aandacht genoot. Over een groep van 160 patiënten, die dit symptomencomplex hadden, waren de verschillende verschijnselen als volgt verdeeld:

Vestibulaire overprikkelbaarheid voor koud water	74 %
Vertigo	63 %
Spontaan miswijzen en (of) abnormaliteiten bij de loopproef en (of) de proef van Romberg	61 %
Nystagmus (in meer dan de helft der gevallen bilateraal, horizontaal	59 %
Laterale blikzwakte	56 %
Hoofdpijn	47 %
Convergentiezwakte	44 %
Waarnemingsdoofheid tengevolge van deficientie	26 %
Reactieve vestibulaire dysharmonie of dissociatie	23 %
Anisocorie	19 %
Symptoom van Eagleton	16 %
Mydrasis	vaak
Oculair tandrad phenomeen van Bing	vaak
Oorsuizen tengevolge van deficientie	14 %
Ataxie van convergentiebewegingen	6 gevallen
Onrondheid der pupillen	een paar gevallen
Positie-nystagmus	een paar gevallen
Oogdeviatie van Hertwig-Magendie	2 gevallen
Visioenen van Pick	2 gevallen

Naast dit syndroom bestonden vele andere verschijnselen, gedeeltelijk anamnestisch, gedeeltelijk ook ten tijde van het onderzoek, en wel:

Hypo- of achloorhydrie	zeer vele gevallen
„Branden" en pijnen in handen en voeten	63 %
Diarrhoe, met remissies en exacerbaties	42 %
Neuritis retrobulbaris	31 %
Perlèche en (of) cheilosis	24 %
Dermatitis van het scrotum	23 %
Nauwe capillairen in het nagelbed	19 %
Ataxie	16 %
Stomatitis, glossitis en (of) pharyngitis	14 %

Het pathologisch-anatomisch substraat van de oto-neurologische afwijkingen is een degeneratieve hersenstam-encephalitis. Nystagmus wordt veroorzaakt òf door laesies van het vestibulaire kerngebied, òf van de fasciculus longitudinalis medialis. Ook laesies hooger in de blikbaan zijn mogelijk.

Bij deze groep van 160 waren toen ter tijd slechts 2 gevallen met typische pellagra-dermatitis, maar dit was pas het tweede jaar der krijgsgevangenschap. Later, toen de omstandigheden in alle opzichten slechter werden en er meer werk buitenshuis en in de zon verricht werd, ontstond veel meer dermatitis. Eén patiënt stierf met een volledig ontwikkeld syndroom van K o r s a k o f f.

Deze afwijkingen worden toegeschreven aan pellagra, waarvan vertigo en vele andere der genoemde symptomen initiale verschijnselen zijn, die lang voordat zich eventueel een dermatitis ontwikkelt, optreden. Pellagra in den zin van de ziekte, zooals deze spontaan voorkomt, als een polydeficientie, waarbij nicotinezuurgebrek een groote rol speelt en zeker vele opvallende en belangrijke symptomen veroorzaakt, maar in welk ziektebeeld gebrek aan andere componenten van het B complex zijn deel bijdraagt.

Zoo is het zeer goed mogelijk, dat riboflavinegebrek de voornaamste rol speelt bij de pathogenese der symptomen van het centrale zenuwstelsel, van de neuritis retrobulbaris en enkele andere begeleidende verschijnselen. Er zijn waar-

nemingen van andere onderzoekers, die voor deze opvatting schijnen te pleiten. Bij de therapie moet men echter het zekere voor het onzekere nemen en zal men zeker geen kwaad doen met alle factoren van het B complex toe te dienen. Onder bepaalde omstandigheden moet toevoeging van ventriculine worden overwogen.

Het belang voor de gematigde klimaten bestaat hierin, dat het syndroom van M é n i è r e veroorzaakt kan worden door initiale en soms nog monosymptomatische pellagra. Bij „idiopathische" duizeligheid, vooral wanneer deze van centralen oorsprong is, moet men naar meerdere beginsymptomen van pellagra speuren en een proeftherapie met B vitaminen inzetten, of althans ernstig overwegen. Misschien zal het mogelijk blijken, op het spoor der juiste aetiologie te komen door het vinden van het karakteristieke oto-neurologische beeld.

Dezelfde redeneering geldt, *mutatis mutandis*, voor perlèche, cheilosis, stomatitis, glossitis, pharyngitis, enz., evenals voor waarnemingsdoofheid en oorsuizen.

SAMEVATTING

Veel simptome van avitaminose het voorgekom onder geallieerdes krygsgevangenes, wat gedurende die jare 1942 tot en met 1945 hul in kampe in die Verre Ooste bevind het. Die voedsel was veral arm aan vitamines van die B tipe, dierlike eiwitte en vette. In later stadia was ook die kalorie waarde onvoldoende. Naas die veel ander simptome het 'n oto-neurologiese syndroom die meeste aandag getrek. Onder 'n groep van 160 pasiënte wat hierdie betrokke simptome getoon het, kon die volgende waargeneem word:

Vestibulêre oorprikkelbaarheid vir koue water.. in	74 %
Vertigo	63 %
Spontane miswysinge en (of) abnormaliteite bij die looptoets en (of) bij die toets van Romberg..	61 %
Nystagmus (in meer dan die helfte van die gevalle bilateraal horisontaal)	59 %
Laterale blikswakte	56 %
Hoofpyne	47 %
Convergensieswakte	44 %
Waarnemingsdoofheid as gevolg van avitaminose..	26 %
Reaktiewe vestibulêre disharmonie of dissosiasie...	23 %
Anisocorie	19 %
Simptoom van Eagleton	16 %
Mydriasis	dikwels
Okulêre tandrad fenomeen van Bing	dikwels
Oorsuisinge as gevolg van avitaminose	14 %
Ataksie van convergensie beweginge.....	6 gevalle
Onrondheid van die pupille	paar gevalle
Posisie nystagmus.....	paar gevalle
Skeelheid van Hertwig-Magendie.....	2 gevalle
Visioene van Pick.....	2 gevalle

Deur ondervraging en deur waarneming gedurende ondersoek kon naas bogenoemde syndroom ook nog die volgende simptome vasgestel word:

Hypo- of achloorhydrie.....	baie gevalle
„Brand" en pyne in hande en voete	63 %
Diarree, met remissies en exaserbasies	42 %
Neuritis retrobulbaris	31 %
Perlèche en (of) cheilosis	24 %
Dermatitis van die scrotum.....	23 %
Nou haarvate in die naelbed	19 %
Ataksie	16 %
Stomatitis, glossitis en (of) pharyngitis	14 %

Die patologies anatomiese ondergrond van hierdie oto-neurologiese afwykinge is 'n encephalitis in die harsingstam met 'n duidelik degeneratiewe karakter. Nystagmus word veroorsaak deur beskadiging van die vestibulêre kerngebied of deur die van die fasciculus longitudinalis medialis. Beskadiging hoër in die blikbaan is ook moontlik.

Ek moet konstateer dat toendertyd, d.w.s. in die tweede jaar van die gevangeskap, slegs twee van die 160 pasiënte die tipiese pellagra dermatitis gehad het; later toe die voedsel posisie versleg en veeleisender werk buitenshuis en in die son verrig moes word, kom daar veel meer gevalle van dermatitis voor. Een pasiënt is oorlede met duidelike simptome van die volledig ontwikkelde syndroom van Korsakoff.

Al bogenoemde afwykinge is veroorsaak deur pellagra. Vertigo en veel ander van die bogenoemde simptome kom reeds aan die begin stadium van pellagra voor, terwyl eers later die werklike dermatitis na vore mag tree.

Pellagra — altans in soverre as dit in die natuur voorkom — is te wyte aan gebrek van meerdere faktore van die B tipe. Gebrek aan nicotine suur speel hierby 'n vername rol en is verantwoordelik vir die navore tree van belangrike simptome. Dit moet egter beklemtoon word dat gebrek aan ander komponente van die B tipe wel deeglijk 'n rol speel.

So is dit byv. goed moontlik dat gebrek aan riboflavine die belangrikste rol speel in die ontstaan van encephalitis, neuritis

retrobulbaris en enkele andere verskynsele. Waarneminge van ander ondersoekers pleit reeds vir hierdie bewering. By die behandeling van dergelike gevalle is ons aan die veilige kant om alle faktore van die vitamine B tipe toe te dien. Die toevoeging hiervan bly in alle gevalle onskadelik vir die pasiënt. Onder bepaalde omstandighede mag die toedien van ventriculine oorweeg word.

Van belang is — en hier dink ons veral aan lande waar pellagra nie endemies is nie — dat die syndroom van Ménière veroorsaak kan word deur pellagra in sy begin stadium, in welke gevalle pellagra monosimptomaties mag wees. In geval van idiopatiese duiseligheid, veral wanneer dit van sentrale oorsprong is, moet na meerdere begin simptome van pellagra gesoek word. Proefbehandeling deur middel van B vitamines is aan te beveel. Miskien sal dit in die toekoms blyk moontlik te wees om op die spoor van die juiste aetiologie te kom, deur die vind van die karakteristieke oto-neurologiese beeld.

Dieselfde aetiologie moet altyd voor oë gehou word — indien geen ander duidelike oorsaak sig vertoon nie — in geval van perlèche, cheilosis, glossitis, stomatitis, pharyngitis, waarnemingsdoofheid, oorsuisinge, e.d.m.

RESUME

De nombreux symptômes de carence ont été observés chez des prisonniers de guerre alliés en Extrême-Orient pendant les années 1942 à 1945 inclus. L'alimentation était très pauvre en vitamines du groupe B, en albumines animales et graisses, et pendant les dernières périodes la teneur en calories était insuffisante aussi. A côté d'un grand nombre d'autres phénomènes, un syndrôme oto-neurologique a été observé, méritant le plus grand intérêt. Sur un groupe de 160 malades présentant cet ensemble de symptômes, les différents phénomènes se répartissent comme suit :

Hyperexcitabilité vestibulaire à l'eau froide	74 %
Vertige	63 %
Anomalies spontanées aux épreuves d'indication et (ou) à l'épreuve de Romberg et (ou) à la marche aveugle	61 %
Nystagmus (dans plus de la moitié des cas bilatéral-horizontal)	59 %
Faiblesse du regard latérogyre	56 %
Céphalées	47 %
Faiblesse de la convergence	44 %
Surdité de perception à la suite de déficiences	26 %
Dysharmonie et dissociation vestibulaires provoquées	23 %
Anisocorie	19 %
Symptôme d'Eagleton (abolition élective du nystagmus rotatoire)	16 %
Mydriase	souvent
Signe oculaire de la roue dentée de Bing	souvent
Bourdonnements d'oreilles à la suite de déficiences	14 %
Ataxie des mouvements de convergence	6 cas
Déformation pupillaire	très peu de cas
Nystagmus de position	très peu de cas

Strabisme de Hertwig-Magendie	2 cas
Visions de Pick	2 cas

A côté de ce syndrôme, il y eut de nombreux autres phénomènes révélés en partie par l'anamnèse, en partie pendant l'examen, à savoir:

Hypo- ou achlorhydrie	très nombreux cas
Sensations de brûlure et douleurs dans les pieds et les mains	63 %
Diarrhée avec rémissions et exacerbations	42 %
Névrite rétrobulbaire	31 %
Perlèche et (ou) cheiloïde	24 %
Erythème scrotal	23 %
Vasoconstriction capillaire des extrémités	19 %
Ataxie	16 %
Stomatite, glossite et (ou) pharyngite	14 %

Le substratum anatomico-pathologique des anomalies oto-neurologiques est une encéphalite dégénérative du tronc cérébral. Le nystagmus est causé par des lésions de la zône nucléaire vestibulaire ou du faisceau longitudinal postérieur. Des lésions localisées plus haut dans le faisceau fronto-oculomoteur sont également possibles.

Parmi ce groupe de 160 malades il n'y avait à ce moment-là que deux cas d'érythème pellagreux caractérisé, mais on n'était encore que dans la deuxième année de la captivité. Plus tard lorsque les conditions de vie empiraient sous tous les rapports et qu'on travaillait plus souvent en plein air et au soleil il y eut beaucoup plus d'accidents cutanés. Un malade mourut avec un syndrôme de Korsakoff entièrement développé.

Ces modifications sont attribuées à la pellagre dont plusieurs des symptômes déjà mentionnés sont des manifestations précoces, accidents qui surviennent longtemps avant l'apparition éventuelle d'un érythème. Il s'agit de la pellagre au sens de la maladie telle qu'elle se rencontre dans la nature, comme une polydéficience dans laquelle le manque d'acide nicotinique joue un rôle important et est certainement à l'origine de

symptômes importants, mais dans le tableau nosologique de laquelle le manque d'autres éléments constitutifs du groupe B a sa part.

Ainsi il est fort possible que le manque de lactoflavine joue le rôle principal dans l'étiologie des symptômes du système nerveux central, de la névrite rétrobulbaire et d'autres phénomènes concomitants. Des observations d'autres chercheurs semblent appuyer cette conception. Mais dans le traitement il faut suivre la voie la plus sûre et l'on ne fera pas mal d'appliquer tous les éléments du groupe B. En certaines circonstances il faut envisager d'y joindre la ventriculine.

L'intérêt que présente l'étude de ces cas pour les zônes tempérées réside en ce que le syndrôme de Ménière peut avoir pour cause une pellagre initiale et quelquefois encore monosymptômatique. Dans les cas de vertige „idiopathique", surtout quand celui-ci est d'origine centrale, il faut chercher à déceler plusieurs symptômes initiaux de pellagre et commencer ou du moins envisager sérieusement une épreuve thérapeutique avec des vitamines B. Peut-être la possibilité se révèlera-t-elle de rendre probable l'étiologie par la découverte du tableau oto-neurologique caractéristique.

La même étiologie doit être envisagée en cas de stomatite, perlèche, cheiloïde, glossite, pharyngite, etc., de surdité de perception et de bourdonnements d'oreilles quand on ne découvre pas de cause manifeste.

ZUSAMMENFASSUNG

In den Jahren 1942—1945 wurden bei alliierten Kriegsgefangenen im Fernen Osten viele Mangelerscheinungen beobachtet. Die Ernährung war sehr arm an Vitaminen der B-Gruppe, tierischem Eiweiss und Fetten, während in den letzten Stadien auch der kalorische Wert unzureichend war. Neben vielen anderen Symptomen wurde ein otoneurologisches Syndrom wahrgenommen, das das grösste Interesse fand. Eine Gruppe von 160 Patienten mit diesem Symptomenkomplex zeigte folgende Verteilung konstituierender Erscheinungen:

Vestibuläre Übererregbarkeit gegen kaltes Wasser	74 %
Schwindel	63 %
Spontane Abnormalitäten bei dem Zeige-, Geh- und (oder) dem Rombergschen Versuch	61 %
Nystagmus (mehr als die Hälfte der Fälle bilateral, waagerecht)	59 %
Schwäche der lateralen Blickbewegungen	56 %
Kopfschmerzen	47 %
Konvergenzschwäche	44 %
Schallempfindungsschwerhörigkeit durch mangelhafte Ernährung	26 %
Reaktive vestibuläre Dysharmonie und Dissoziation	23 %
Anisokorie	19 %
Eagletonsches Zeichen	16 %
Mydriasis	oft
Oculäres Zahnradphänomen von Bing	oft
Ohrengeräusche durch mangelhafte Ernährung	14 %
Ataxie der Konvergenzbewegungen	6 Fälle
Abweichungen der Pupillenform	einige Fälle
Lagenystagmus	einige Fälle
Hertwig-Magendiesche Vertikaldivergenz	2 Fälle
Pick sche Visionen	2 Fälle

Neben diesem Syndrom kamen viele andere Erscheinungen vor, teils anamnestisch, teils zur Zeit der Untersuchung:

Hypo- oder Achlorhydrie	sehr viele Fälle
„Brennen" und Schmerzen der Hände und Füsse	63 %
Diarrhoea, in Schüben	42 %
Retrobulbäre Neuritis	31 %
Perlèche und (oder) Cheilosis	24 %
Skrotale Dermatitis	23 %
Enge Kapillaren im Nagelbett	19 %
Ataxie	16 %
Stomatitis, Glossitis und (oder) Pharyngitis	14 %

Das pathologisch-anatomische Substrat der otoneurologischen Symptome ist eine degenerative Hirnstammencephalitis. Nystagmus wird teils durch Läsionen in dem vestibulären Kerngebiet, teils durch solche in dem hinteren Längsbündel hervorgerufen. Auch Schädigungen höher in der Blickbahn sind nicht ausgeschlossen.

In dieser Gruppe von 160 Patienten waren seinerzeit, im zweiten Jahr der Gefangenschaft, nur 2 mit typischer Pellagradermatitis. Später, mit zunehmender Verschlechterung der Umstände und Arbeitsleistung im Freien und an der Sonne trat Dermatitis viel häufiger auf. Ein Patient starb mit vollständig ausgeprägtem Korsakoff-Syndrom.

Diese Abweichungen werden der Pellagra zugeschrieben, die Vertigo und viele andere der genannten Symptome zu initialen Erscheinungen haben kann, längere Zeit, bevor sich eine eventuelle Dermatitis entwickelt. Bei der spontan vorkommenden Pellagra, einer multiplen Mangelkrankheit, wobei Nikotinsäuremangel eine grosse Rolle spielt und sicher viele auffallende und wichtige Symptome bedingt, ist jedoch auch ein Defizit anderer Komponenten der B-Gruppe fraglos bedeutungsvoll.

So ist es möglich, dass Laktoflavinmangel bei der Pathogenese der Symptome des Zentralnervensystems, der retrobulbären Neuritis und einiger anderen Begleitsymptome die wichtigste Rolle spielt. Wahrnehmungen anderer Forscher sprechen gleichfalls für diese Auffassung. Auf Grund dessen

wird man gut daran tun, bei der Therapie alle Faktoren der B-Gruppe zu verabreichen. In bestimmten Fällen soll die zusätzliche Applikation von Ventrikulin erwogen werden.

Bedeutungsvoll für die gemässigten Zonen ist, dass das Ménière sche Syndrom durch initiale und zuweilen erst monosymptomatische Pellagra bedingt werden kann. Bei „idiopathischem" Schwindel, besonders zentraler Natur, soll man nach weiteren Initialsymptomen der Pellagra fahnden und eine Probetherapie mit B-Vitaminen ernstlich erwägen, bzw. beginnen. Möglicherweise wird das Feststellen des charakteristischen otoneurologischen Bildes zu der richtigen Aetiologie führen können.

Dieselbe Aetiologie soll erwogen werden in Fällen von Perlèche, Cheilosis, Stomatitis, Glossitis, Pharyngitis, usw., Schallempfindungsschwerhörigkeit und Ohrengeräuschen, falls keine bestimmte Ursache gefunden wird.

BIBLIOGRAPHY

1. Alexander, L., Pijoan, M. and Myerson, A. Beriberi and Scurvy, Tr. Am. Neurol. A. 64, 135, '38.
1a. Andrews, G. C. Diseases of the Skin, Saunders & Co., '46.
2. Atkinson, M. A simple quantitative method of testing vestibular function, Arch. Otolar. 30, 6, 916, Dec. '39.
3. ——, Observations on the etiology and treatment of Ménière's syndrome, J. A. M. A. 116, 16, 1753, Apr. '41.
4. Aubry, M. Oto-neurologie, Masson & Cie, '44.
5. Ballenger, W. L. and Ballenger, H. Ch. Diseases of the Nose, Throat and Ear, '38.
6. Ballif, L., Lwoff, A., Querido, A. and Ornstein, I. La nicotinamidémie chez les pellagreux, Compte Rendu Soc. Biol. 131, 903, '39.
7. Bean, W. B., Vilter, R. W. and Spies, T. D. Meeting Chicago Nov. 1, 2, Centr. Soc. Clin. Research, J. A. M. A. 116, 21, 2427.
8. Beattie, J. M. and Dickson, W. E. C. A Textbook of Pathology, '43.
9. Beckh, W., Ellinger, P. and Spies, T. D. Porphyrinuria in Pellagra, Quart. J. Med. 6, 305, '37.
10. Bender, L. and Schilder, P. Encephalopathia alcoholica, Arch. Neur. Psych. 29, 900, May '30.
11. Bicknell, F. and Prescott, F. The Vitamins in Medicine, '46.
12. Bielschowsky, A. Symptomatologie der Störungen im Augenbewegungsapparat, Handb. Neurol. Bumke und Förster, IV, 173, '36.
13. Bing, R. Textbook of Nervous Diseases, '40, and German Edition '45.
14. Bothman, L. and Crowe, S. J. The 1940 Yearbook of the Eye, Ear, Nose and Throat.
15. Brickner, R. M. and Brill, N. Q. Dietetic and related studies on multiple sclerosis, Arch. Neur. Psych. 46, 16, '41.
16. Brunner, H. Allgemeine Symptomatologie des Nerv. Vestibularis usw. Handb. Neurol. des Ohres, Alexander und Marburg, I, '24.
17. Burger, H. Oor-, Neus- en Keelziekten, '38.
18. Burgess, R. C. Deficiency diseases in prisoners-of-war at Changi, Singapore, Lancet, 2, 12, Sept. '46.
19. Cambrelin, G. Le cervelet et les voies vestibulaires, Acta Oto-Lar. 27, 359, '39.
20. Castellani, A. and Chalmers, A. J. Manual of Tropical Medicine, '19.
21. Ceelen, W. Über Darmveranderungen bei Pellagra, Beitr. Path. Anat. und allg. Path. 87, 2, 488, '31.
22. Chotzen, F. Zum Auftreten pellagröser Erkrankungen in Deutschland, Zeitschr. ges. Neurol. und Psych. 109, 739, '27.
23. Couchoud, P. L. Le Kubisagari (maladie de Gerlier), Revue de Médecine, 34, 241, Avr. '14.
24. Crinis, M. de. Über Schwerhörigkeit für Sprache bei erhaltenem Tongehör, Arch. f. Ohren usw. Heilk. 149, 103, '41.

25. Cruickshank, E. K. Painful feet in P. O. W. s in the Far East, Lancet, 2, 9, 369, Sept. 14, '46.
26. Cunningham, D. J. Textbook of Anatomy, '37.
27. Deinse, J. B. Het Ménière syndroom, Thesis University of Amsterdam, June 6, '46.
28. Dekking, H. M. Over Kampoogen, Ned. Tijdschr. v. Geneesk. I, 11/12, 216, March '46.
29. Denton, J. The Pathology of Pellagra, Am. J. Trop. Med. 5, 2, 173, March '25.
30. Dorland, W. A. N. The American illustrated Medical Dictionary, '45.
31. Dorochenko, I. T. De l'état des voies aériennes supérieures chez les malades atteintes de pellagre, Acta Oto-Lar. 26, 658, '38.
32. Dumoulin, F. V. B. Deficientieverschijnselen onder geallieerde krijgsgevangenen in Siam, Ned. T. v. G. 90, 3, 31, 925, Aug. 3, '46.
33. Eddy, W. H. and Dalldorf, G. The Avitaminoses, '44.
34. Ellinger, P., Coulson, R. A. and Benesch, R. Production and release of nicotinamide by the intestinal flora in man, Nature, 154, 270, '44.
35. Elvehjem, C. A., Madden, R. J., Strong, F. M. and Woolley, D. W. Relation of nicotinic acid and nicotinic amid to canine black tongue, J. Am. Chem. Soc. 59, 1767, '37.
36. Field, H., Melnick, D., Robinson, W. D. and Wilkinson, C. F., Studies on the chemical diagnosis of pellagra (nicotinic acid deficiency), J. Clin. Invest. 20, 379, July '41.
37. Fisher, G. E. The oesophageal manifestations in pellagra, South. Med. J. 37, 446, '44.
38. Frenzel, H. Nystagmus als Hirnsymptom, Passow Schaefer Beitr. 28, 38 and 221, '31.
39. Frostig, J. P. and Spies, T. D. The initial nervous syndrome of pellagra and associated deficiency diseases, Am. J. Med. Sci. 199, 2, 157, Febr. '40.
40. Fürstenberg, A. C., Lashmet, F. H. and Lathrop, F. Ménière's symptom complex, Ann. Otol. Rhin. Lar. 43, 1035, Dec. '34.
41. Gillman, T. and Gillman, J. Treatment of infantile pellagra, Lancet, 2, 13, 446, Sept. 28, '46.
42. Goldberger, J. and Wheeler, G. A. Experimental pellagra in the human subject etc. Publ. Health Rep. U. S. A. 30, 3336, '15.
43. —— and Tanner, W. F. A study of the pellagra preventing action of dried beans, casein, dried milk and brewers' yeast, Publ. Health Rep. 40, 54, '25.
44. ——, Pellagra, In Tice: Practice of Medicine, 9, 225, '31.
45. Grinker, R. R. Neurology, '43.
46. Güttich, A. Zur vestibulären Symptomatologie der Hirnstammerkrankungen, Arch. Ohren usw. Heilk. 147, 250, '40.
47. Hallpike, C. S. and Cairns, H. Observations on the pathology of Ménière's syndrome, Proc. Roy. Soc. Med. 31, 1317, Sept. '38.
48. Harris, H. E. and Moore, P. M. The use of nicotinic acid and thiamin chloride in the treatment of Ménière's disease, Med. Clin. N. Am. 24, 533, March '40.
49. Harrison, G. F. Nutritional deficiency, painful feet, high blood pressure in Hongkong, Lancet, 1, 26, 961, June 29, '46.
50. Herzenberg, H. Pellagra, Beitr. zur Path. Anat. und allg. Path. 96, 1, 97, '35.
51. Jolliffe, N., Bowman, K. M., Rosenblum, L. A. and Fein, H. D. Nicotinic acid deficiency encephalopathy, J. A. M. A. 114, 4, 307, Jan. '40.
52. ——, Wortis, H. and Fein, H. D. Wernicke syndrome, Arch. Neurol. and Psych. 46, 4, 569, Oct. '41.

53. Justin-Besançon, L. and Lwoff, A. Vitamine antipellagreuse et avitaminoses nicotiniques, Masson & Cie, '42.
54. Kinnier Wilson, S. A. Neurology, '40.
55. Klestadt, W. Symptomatologie der Erkrankungen des N. VIII usw. Handb. der Neurol. Bumke u. Förster, 4, 359, '36.
56. Kleyn, A. de, and Versteegh, C. Schwindelanfälle und Nystagmus bei einer bestimmten Lage des Kopfes, Acta Oto-Lar. 6, 99, '24.
57. —— and Versteegh, C. Some experimental remarks on Ménière's disease, Acta Oto-Lar. 6, 38, '24.
58. —— and Nieuwenhuyse: Schwindelanfälle und Nystagmus bei einer bestimmten Stellung des Kopfes, Acta Oto-Lar. 11, 155, '27.
59. ——, Einige experimentell-klinische Bemerkungen über die kalorische Reaktion, Arch. f. Ohren usw. Heilk. 122, 169, '29.
60. ——, Vestibulaire reacties bij latenten nystagmus, N. T. v. G. 83, 3645, '39.
61. ——, Positienystagmus tengevolge van halsreflexen, in het bijzonder bij arachnoiditis posterior, N. T. v. G. 85, 316, '41.
62. ——, Plotselinge geheele of gedeeltelijke uitschakeling van het octavussysteem bij schijnbaar normale personen, N. T. v. G. 85, 891, '43.
63. ——, War-experiences from the Oto-Rhino-Laryngological Clinic, Acta Oto-Lar. 34, 2—3, 99, '46.
64. Kodicek, E., Carpenter, K. J. and Harris, L. J. "Pellagragenic" activity of indole-3-acetic acid in the rat, Lancet, 2, 14, 491, 5 Oct. '46.
65. Kuilman, J. Kampduizeligheid, Paper read for the Neth. O. R. L. Ass. at Groningen, 1 July '46.
66. ——, Kampduizeligheid, Ned. Tijdschrift v. Geneesk. 90, III, 33, 1000, 17 Aug. '46.
67. Langworthy, O. R. Lesions of the central nervous system, characteristic of pellagra, Brain, 54, 291, '31.
68. ——, Der Schwindel, Handb. der Neurol. des Ohres, Alexander und Marburg, 1, 553, '26.
69. Leidler, R. Wie weit kann man aus der Vestibularuntersuchung auf Art und Sitz einer Hirnerkrankung schliessen? Pract. Otorhinolar. 2, —, 86, May 1939 and 2, —, 152, July 1939.
70. Lewy, F. H., Spies, T. D. and Aring, C. D. The incidence of neuropathy in pellagra, Am. J. Med. Sci. 199, 6, 840, June '40.
71. Lundh, B. and Geill, T. Riboflavin-Avitaminosis, Acta Med. Scand. 110, II/III, 172, '42.
72. Lwoff, A., Querido, A., Digonnet, L. and Garnier, Mlle. La nicotinamidémie chez les femmes gravides, C. R. Soc. Biol. 131, 900, '39.
73. Manen, J. G. van, De behandeling van kampoogen (deficientie-amblyopie), N. T. v. G. II, 26, 733, June 1946.
74. Manson Bahr, Ph. Tropical diseases 1940.
75. Melnick, D., Robinson, W. D. and Field Jr. H. Influence of the excretion of other pyridine compounds upon the interpretation of the urinary nicotinic acid values, J. Biol. Chem. 136, 131, '40.
76. ——, ——, and ——, Urinary excretion of nicotinic acid and its derivatives by normal individuals, J. Biol. Chem. 136, 145, '40.
77. Meyer, A. Parenchymatous systemic degenerations mainly in the central nervous system, Brain, 24, 47, '01.
78. Mohr, J. Verbal informations in P. O. W. camp Batavia, '44.
79. Monteiro, M. A., Coutinho, H., Janz, G. J. and Loureiro, J. A. de, Endemic pellagra in Northern Portugal, J. Hygiene, 44, 6, 518, Sept. '46.

80. Moore, F. Nutritional retrobulbar neuritis, Lancet, 2, 7, 246, Aug. 17, '46.
81. Moore, M. T., Treatment of multiple sclerosis with nicotinic acid and vitamin B_1, Arch. Int. Med. 65, 1, '40.
82. Moore, R. A., Spies, T. D. and Cooper, Z. K. Histopathology of the skin in pellagra, Arch. o. Derm. a. Syph. 46, 1, 100, July '42.
83. Moorrees, H. Retrobulbaire neuritis, papers read in P. O. W. camp Pakan Baroe 1945.
84. Najjar, V. A. and Holt, E. M. The excretion of specific fluorescent substances in the urine in pellagra, Science, 93, 20, '41.
85. Niles, G. M. Pellagra, The Practice of Medicine in the Tropics, Byam and Archibald, 3, '23.
86. Nylen, C. O., Some cases of ocular nystagmus due to certain positions of the head, Acta Oto-Lar. 6, 38, '24.
87. ——, Kopfstellungsnystagmus, Acta Oto-Lar. 11, 147, '27.
88. ——, Einiges über die Entwicklung der klinischen Vestibularis-Forschung während der letzten 25 Jahre, usw., Acta Oto-Lar. 31, 223, '43.
89. Ohm, J. Das Augenzittern der Bergleute, Handb. der Neurol. des Ohres, Alexander und Marburg, III, 509, '26.
90. Pavlov, I. P. Conditioned reflexes, Oxford University Press, London, '27.
91. Petri, S., Norgaard, F. and Bandier, E. Studies on the effect of nicotinic acid upon experimental gastroprival pellagra, Acta Med. Scand. 98, 113, Dec. '38.
92. Piersol, G. A. Human Anatomy, '30.
93. Querido, A., Albeaux-Fernet, M. and Lwoff, A. La nicotinamidémie normale et pathologique, C. R. Soc. Biol. 131, 903, '39.
94. ——, Over nicotinezuurdeficientie, Voeding, 6 Febr. '42.
95. ——, Over nicotinezuur en pellagra, to be published in the Ned. T. v. G.
96. Raadt, O. L. E. de, Oto-neurological disturbances caused by deficiency, Paper read in P. O. W. camp Bandoeng, July 20, '43.
97. ——, Oto-neurologische en andere stoornissen bij initiale pellagra, Paper read before the Neth. Ass. Trop. Med. Amsterdam, Sept. 29, '46.
98. ——, Initial oto-neurological disturbances in pellagra, to be published in Acta Oto-Lar.
99. Ranson, S. W. The Anatomy of the Nervous System, '43.
100. Rehsteiner, K. Erneutes Auftreten der Gerlier'schen Krankheit, Schweiz. Med. Wochenschr. 55, 19, '25.
101. Riordan, T. J., Gellis, S. and Rubinowitz, A. M. Unusual sites of lesions in pellagra, Arch. Derm. a. Syph. 46, 5, 661, Nov. '42.
102. Roch, M. De la maladie de Gerlier à l'encéphalite épidémique, Presse Médicale 17, 195, 323, Févr. '32.
103. Ruffin, J. M. Diagnosis and treatment of mild vitamin deficiencies, J. A. M. A. 117, 1493, '41.
104. Scheibe, A. Die Krankheiten der Ohrtrompete, Handb. der Hals usw. Heilk. Denker und Kahler, 7, '26.
105. Schoonhoven van Beurden, A. J. R. E. van, Behandeling van acrodynie met nicotinezuur, N. T. v. G. 49, 4793, 7 Dec. '40.
106. Schwartz, J. Neuropathia Nervi Optici, Papers read in P. O. W. camp Bandoeng '42 and '43.
107. Scott, H. H. An investigation into an acute outbreak of central neuritis, Ann. Trop. Med. Parasit. 12, 109, '18.
108. Sebrell, W. H. Vitamins in relation to the prevention and treatment of pellagra, J. A. M. A. 110, 1665, May 14, '38.

109. Selfridge, G. Eighth nerve high tone deafness from a nutritional standpoint, Ann. Otol. Rhin. Lar. 46, 93, March '37.
110. ——, Nicotinic acid and the eighth nerve, Ann. O. R. Lar. 48, 39, March '39.
111. ——, The eighth nerve in relation to thiamin chloride and nicotinic acid, Ann O. R. Lar. 48, 419, June '39.
112. Simons, R. D. G. Ph. Dermatoses in tropenkrijgsgevangenschap, N. T. v. G. 90, 16, 352, 20 Apr. '46.
113. Simpson, J. "Burning Feet" in British P. O. W. s in the Far East, Lancet, 1, 26, 959, June 29, '46.
114. Singer, D. and Pollock, L. J. The histopathology of the nervous system in pellagra, Arch. Int. Med. 11, 6, June '13.
115. Soewarno, M. Iets over kampoogen, N. T. v. G. 1, 11/12, 213, March '46.
116. Spatz, H. Anatomie des Mittelhirns, Handb. Neurol. Bumke und Förster, 1, '35.
117. Spies, T. D. Effect of folic acid on persons with macrocytic anaemia in relapse, J. A. M. A. 130, 474, Febr. 23, '46.
118. ——, Bean, W. B. and Stone, R. E. The treatment of subclinical classic pellagra etc. J. A. M.A. 111, 584, Aug. 13, '38.
119. ——, Aring, C. D., Gelperlin, J. and Bean, W. B. The mental symptoms of pellagra, their relief with nicotinic acid, Am. J. Med. Sci. 196, 461, Oct. '38.
120. ——, Bean, W. B. and Ashe, W. F. Recent advances in the treatment of pellagra and associated deficiencies, Ann. Int. Med. 12, 1830, May '39.
121. ——, Bean, W. B. and Ashe, W. F. A note on the use of vit. B_4 in human nutrition, J. A. M. A. 112, 23, 2414, June '39.
122. ——, Bean, W. B., Vilter, R. W. and Huff, N. E. Endemic riboflavin deficiency in infants and children, Am. J. Med. Sci. 200, 5, 697, Nov. '40.
123. Stannus, H. S. Pellagra and pellagra-like conditions in warm climates, Trop. Dis. Bull. 33: 10, 729, Oct.; 11, 815, Nov.; and 12, 885, Dec. '36.
124. ——, Pellagra, Lancet, 1, 352, '40.
125. ——, Some problems of Riboflavin and allied deficiencies, Lumleian Lectures, Brit. Med. J. 2, 103, '44.
126. Stare, F. J. The cecal flora and nicotinic acid synthesis, Nutritional reviews, 4, 3, March '46.
127. ——, Urinary coproporphyrin in nonalcoholic pellagrins, Nutritional reviews, 4, 4, Apr. '46.
128. Stepp, W. und Kühnau, J. Die Vitamine und ihre klinische Anwendung, '39.
129. Stern, F. Multiple Sklerose, Handb. Neurol. des Ohres, Alexander und Marburg, II, 2, 1014, '26.
130. Stevenson, L. D., Mc Gowan, L. E. and Allen, A. M. Changes in the brain in alcoholics, Arch. Neur. a. Psych. 45, 1, 56, Jan. '41.
131. Streit, H. Abweichungen vom normalem Verhalten bei Prüfungen des statischen Apparates usw. Arch. Ohren usw. Heilk. 104, 1/2, 56, Aug. '19.
132. Struycken, H. J. L. Die obere Hörgrenze für Luft- und Knochenleitung, Passow Schaefer Beitr. 3, 406, '10.
133. Sydenstricker, V. P., Sebrell, W. H., Cleckley, H. M. and Kruse, H. D. The ocular manifestations of Ariboflavinosis, J. A. M. A. 114, 2437, '40.
134. ——, Kelly, A. R. and Weaver, J. W. Ariboflavinosis, South. Med. J. 34, 2, 165, Febr. '41.
135. ——, Clinical manifestations of nicotinic acid and riboflavin deficiency (Pellagra), Ann. Int. Med. 14, 1499, '41.
136. ——, The neurological complications of malnutrition, Proc. Roy. Soc. Med. 36, 4, 169, Febr. '43.

137. Tendeloo, N. Ph. Grondbeginselen der Algemeene Ziektekunde, '26.
138. Utermöhlen, G. H. Het prisma effect bij de ziekte van Ménière, N. T. v. G. 85, 1, 12, 1183, March '41.
139. Valkenburg, C. T. Het syndroom van Ménière bij jonge menschen, N. T. v. G. 86, 3, 35, 2179, Aug. 29, '42.
140. Vedder, E. B. Pellagra, Clinical Tropical Medicine, Bercovitz, 618, '44.
141. Watson, C. J. and Layne, J. A. Studies of urinary pigments in pellagra and other pathological states, Ann. Int. Med. 19, 183, 200 and 206, '43.
142. Wechsler, I. Textbook of Neurology, '40.
143. Wright, E. J. Letter to the Editor, Nutritional retrobulbar neuritis, Lancet, 2, 11, 400, Sept. 14, '46.
144. Youngerman, W. M. Kommt Spontannystagmus bei Gesunden vor? Arch. Ohren usw. Heilk. 136, 4, 314, Oct. '33.
145. Zwaardemaker, H. en Quix, F. H. Spraakgehoor, Onderz. Physiol. Lab. Utrecht (5).

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