# SENSORY NEURAL DEAFNESS IN PELLAGRA

By A. YASSIN and M. TAHA (Cairo)*

PELLAGRA is a disorder chiefly found among maize-eaters in countries adjacent to the Mediterranean and Black Seas with high incidence in Egypt. Its incidence among Egyptians was recorded to be 35–65 per cent. in 1898 (Sandwith) and 0·5 per cent. in 1954 (Richard *et al.*).

In 1914 Fink suggested a dietary deficiency evidenced by feeding experiments in human volunteers. Spies holds that there are well-defined syndromes distinguishable in the clinical picture. The first is attributable to nicotinic acid deficiency and accounts for the skin, oral, alimentary and mental derangement and for the vulvar and perineal affections. The second is a deficiency of riboflavin and $B_6$ which are responsible for red, shiny lips, for excoriations at the angles of the mouth, eyes and nostrils and the seborrhœic scaly skin changes found about the nasolabial folds, bridge of the nose and forehead. They are responsible partly for the glossitis and dermatitis. The third are the neuritic manifestations, which are due to lack of vitamin $B_1$. In addition to the B vitamins it is obvious that the dietary inadequacy of pellagrins will give rise to insufficiency of other essential nutrients and in this respect a depletion of vitamin C reserves, proteins, iron, etc., may coexist, but not ætiologically (Mousa *et al.*, 1960).

## Neurological Manifestations of Pellagra

Symmetrical, scattered lesions may be demonstrated in the lateral and posterior columns of the spinal cord associated with myelin degeneration, the cells of Clarke's column may also be affected. There is some resemblance to the pathological picture of subacute combined degeneration of the cord. The cells of the posterior root ganglion demonstrate chromatolysis. Demyelination of the peripheral nerves may be seen, the distal portions tending to be least affected. Degenerative lesions of the blood vessels of C.N.S. are described.

Clinically the common subjective neurological phenomena are paræsthesia, headache, cramps, pains in various parts of the body and muscle weakness. A peripheral neuritis may be the presenting lesion and is associated with burning sensations in the hands and feet, muscular

* From the Otology Section, Kasr El Aini Faculty of Medicine, Cairo University.



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asthenia and wasting, hypotonicity, ataxia and reduction or loss of reflexes. Combinations of peripheral nerve and spinal cord lesions are found, demonstrating different intermediate grades of the two types of lesions. Involuntary movements have been often demonstrated, tremors especially of tongue and face, chorea or athetosis. Any of the cranial nerves may be affected, but this is of infrequent occurrence (Mousa *et al.*, 1960).

Calderini (1847) was the first to record the failing vision, diplopia and vertigo among pellagrins. Although optic neuritis among a good number of pellagrins was observed by Bietty (1901) yet he failed to find any visual field defect.

Procopui (1903) mentioned the frequency of amblyopia in pellagra.

Tinnitus was found in 23·6 per cent. of cases studied in the Neurology Section, Kasr El Ainy Hospital, Cairo (Elwan, 1959), but he could not demonstrate solid evidence of nerve deafness. No incidence of vertigo was reported.

Vibration sense was found affected in 21·8 per cent. of cases among the series of the Neurology Section.

Elwan concluded that tinnitus was a common symptom among Egyptian pellagrins.

Roberts (1912) states that roaring noises in the ears indicate involvement of the auditory nerve.

### Literature on Auditory Dysfunction in Pellagra

The literature on this subject is extremely inadequate. Revising the literature in the last 30 years one could only come across the work done by Church (1933) in England, Cody (1932), Covell (1937), Selfridge (1937 and 1939), and Denny-Brown (1947) in the United States, and de Raadt (1947) in Holland, and Ono (1928) in Japan.

The effect on man of deprivation of vitamin B is well described by Denny-Brown (1947) who examined 3,667 prisoners of war. In his own cases he found 303 men with neurological conditions of whom 13 were found to be deaf. It was often associated with retrobulbar neuritis and ataxia of spinal or bulbar origin. It was not complete in any case; it was usually accompanied by tinnitus, but never by vertigo. The onset was always relatively sudden after a long period of latency, usually months or years after other symptoms without any change in the retrobulbar neuritis or ataxia. The period of latency and limitation of degree was a remarkable feature of all the neuropathies of nutritional origin. The onset was only a subacute progression, however, and did not indicate a direct vascular disorder. Denny-Brown gives these figures:

Among 126 cases neurologically affected he found:

(*a*) Retrobulbar neuritis only .. .. .. .. 73 cases



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(*b*) Retrobulbar neuritis and paræsthesia .. .. 24 cases

(*c*) Retrobulbar neuritis and nerve deafness .. .. 12 cases

(*d*) Retrobulbar neuritis and nerve deafness and ataxia 10 cases

(*e*) Ataxia only .. .. .. .. .. .. 4 cases

(*f*) Retrobulbar neuritis, ataxia and vocal cord paralysis 3 cases

Grande and Paraita in 3,116 patients in Madrid during the Civil War, found that 15 per cent. were nerve deaf.

De Raadt (1947) noticed that the classical works about pellagra did not mention either the complete neurological syndromes, or the otolaryngological manifestations related to this disease.

Having lived in Sumatra and Jawa a long period during the last World War, he studied more than 160 cases suffering from this disease, he proved that these manifestations are more frequent than is generally believed. Among the otological disturbances, one of the most frequently observed is vestibular hyperexcitability, mostly for cold water, this was in 74 per cent. of the cases studied. All types of vertigo were noticed in about 63 per cent. of cases. A typical Ménière's syndrome has been observed: Spontaneous nystagmus in 59 per cent. of cases; spontaneous abnormalities of gait in 61 per cent. of cases; weakness of the lateral gaze and headache in 47 per cent. of cases. Perceptive type of hearing loss was found in many cases; tinnitus in only 4 per cent. of cases. One patient of his series died of real Korsakof syndrome. He attributed these symptoms to degeneration in the brain stem, and he attributed nystagmus to degeneration in vestibular nuclei, and in some cases by disturbances in the posterior longitudinal bundle.

Of the group of 160 patients, only 33 had normal hearing. There were 19 cases of conductive deafness, 15 of mixed type, and 93 of perceptive type. Deafness was almost always bilateral and it seems that this disability was often of slight or moderate intensity. Otoscopy did not reveal serious lesions of the drums, he sometimes found congestion of the Eustachian tubes. The palate, fauces and uvula were angry red.

Covell (1937) studied the histopathological changes within the various structures of the cochlea and cochlear nerve (in rats and chicks) that resulted in the use of such different experimental agents as effect of drugs and various deficiency states. He has shown that the external hair cells, the external sulcus cells, also those of the stria vascularis are susceptible to the action of many drugs such as quinine, salicylates and heavy metals, as well as many deficiency states.

Myelin sheath degeneration of the VIIIth nerve was found to occur especially in the basal and middle turns of the cochlea. Each of the vitamins studied (A, $B_1$, nicotinic acid, $B_6$ and C) showed some degree of myelin degeneration of the cochlear nerve and the cochlea which was



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significant in its variation from the findings of the animals maintained on normal and adequate diets. In the different factors of vitamin B deficiency, the degeneration of the hair cells was one of the chief pathological findings, the other change was a demyelinization of the cochlear nerve, especially in the basal and middle turns of the cochlea. These changes were more pronounced with nicotinic acid deficiency than that observed with the other factors.

Certain factors may act directly to produce change or act indirectly through the vascular supply (the endothelium of the smooth capillaries is affected) or a contraction occurs in the blood vessels which leads to ischæmia and subsequent degeneration of ganglion cells.

Selfridge (1939, 1940) made a comparative study of the relation of the VIIIth nerve to thiamin hydrochloride and nicotinic acid and the relation of urine output of vitamin $B_1$ and porphyrin to deafness. In several cases of nerve deafness he found that vitamin $B_1$ output was as low as 25 per cent. of the normal, in addition he found excess of porphyrin in fully 50 per cent. of the cases. He treated 30 cases of perceptive deafness to whom nicotinic acid, nicotinamide or sodium nicotinate was given in the treatment. The dosage varied from 30–120 mg. t.d.s. The improvement in some cases was striking, especially in bone conduction curves. These substances were used for several months with frequent audiograms done, and when the hearing curves appeared stationary, thiamin hydrochloride was added and additional improvement in hearing was noticed. He also reported improvement in tinnitus in 50 per cent. of the cases. In all these cases $B_1$ output in urine was low and porphyrin was in excess in 50 per cent. of the cases. He concluded that while nicotinic acid cured the skin and mucous membrane involvement in pellagra, the addition of thiamin hydrochloride is necessary to cure the neurological involvement.

## Present Study

Twenty-five pellagrins were studied in the Otology Section, Kasr El Aini Hospital, the age group was selected to be between the second and third decade of life; both extremes of age were discarded to avoid the common causes of local ear disease in childhood and exclude the factor of presbyacusis in old age. All cases were examined neurologically to determine the extent of the neurological manifestations of the disease, and cases with evident middle-ear pathology were dropped from the study.

Pure tone audiometry and cold caloric tests were done in every case.

## Neurological and Otological Findings

1. *Neurological affection*

Twenty-three patients out of 25 were found to have evidence of neurological affection in the form of:



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(*a*) Pain and paræsthesia (peripheral anæsthesia or hypothesia or sometimes hyperthesia).

(*b*) Hyperreflexia in 16 cases (64 per cent.).

(*c*) Diminished vibration sense in five cases (20 per cent.).

(*d*) Mental disorders in three patients (12 per cent.).

(*e*) Cranial nerves (other than the VIIIth nerve) none showed clinical abnormality.

(*f*) Two cases did not show neurological manifestation, but only cutaneous and gastro-intestinal signs.

(*g*) Abnormalities of gait in only one case (4 per cent.).

2. *Otological findings*

(*a*) Normal findings in the external and middle ear, apart from marked whitening of the drum membrane in some cases.

(*b*) Perceptive deafness, seven cases (28 per cent.).

(*c*) Vertigo, four cases (16 per cent.).

(*d*) Tinnitus, five cases (20 per cent.).

(*e*) No spontaneous vestibular phenomena were seen.

Here it is important to stress the difference between vertigo of labyrinthine origin, and that from brain stem lesions. Vertigo of labyrinthine origin is paroxysmal in nature, usually sudden and maximal, and it subsides gradually. Vertigo resulting from brain stem lesions is by contrast more continuous and is made worse by movements, and may persist for hours or even a day.

Both labyrinthine and central vertigo may be related to change of posture, but this is more common in the central form.

## Pure Tone Audiometric Results

1. Four cases showed completely normal threshold, or at most 15 db. loss from the threshold, this was considered to be normal (16 per cent.).

2. Ten cases showed loss of 15 db. in all frequencies, but loss of 20–25 db. in two frequencies (40 per cent.).

3. Four cases showed loss of 25 db. in more than two frequencies (16 per cent.).

4. Seven cases showed loss of 25–40 db. or more in more than two frequencies. This was considered marked impairment of hearing (28 per cent.).



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### Differential Loss of Hearing

Differential loss of hearing was found to be as follows:

| | | |
|---|---|---|
| All tones | 21 cases | 84 per cent. |
| Low tones (most) | 1 case | 4 per cent. |
| Low and Middle tones (most) | 13 cases | 52 per cent. |
| Middle tones only | Nil | |
| Middle and High tones | 8 cases | 32 per cent. |
| High tones only | 1 case | |

*N.B.*: (1) The figures given are for the air conduction curves.

(2) Hearing impairment in all the cases was found to be bilateral and almost symmetrical in both ears.

(3) The loudness recruitment phenomenon could not be elicited by the conventional audiometer available to us, since deafness in the cases described is bilateral and almost symmetrical.

### Treatment

Half the cases received nicotinic acid in doses of 100 mg. by intramuscular injection twice daily for 3–4 days, then a maintenance dose of 50 mg. tablets t.d.s. until all neurological and skin manifestations disappeared. The other half received nicotinic acid amide injections and maintenance in the same dosage. Serial pure tone audiograms were taken just after admission to the hospital, after 7 and 21 days. Fading of skin and mucous membrane lesions occurred in 3–4 days in nearly all the cases. Skin pigmentation when present did not disappear. The neurological manifestations took a longer time to disappear usually from 15–20 days. Disappearance of neurological manifestations was taken to be a sure criterion of cure.

### Clinical and Audiometric Findings after Treatment

Improvement of 10 db. is dropped as being insignificant.

We got improvement of 15–20 db. in different frequencies in four cases, viz.:

Improvement of 15–20 db in three frequencies (250, 500 and 1,000) in one case (4 per cent.). Case No. I.

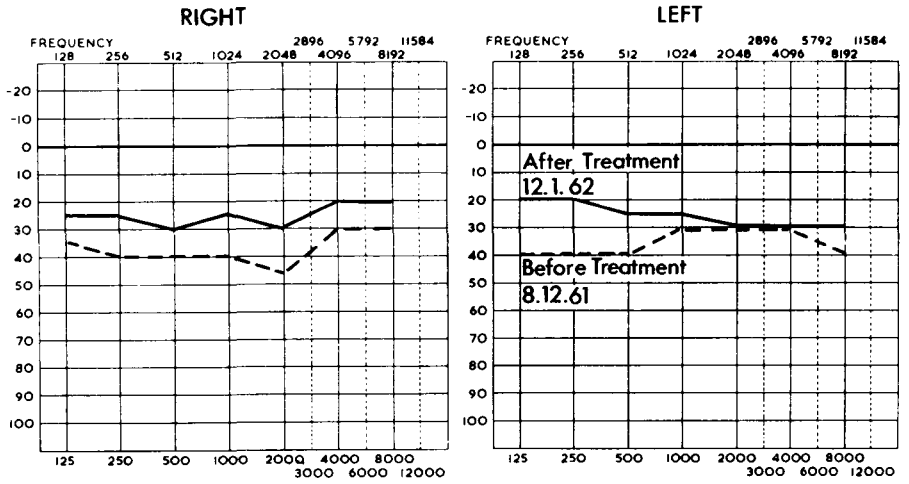
Improvement of 15–25 db. throughout the whole scale, but mainly middle and high tones (500, 1,000, 2,000, 8,000) in one case (4 per cent.). Case No. II.

Improvement of 15–25 db. mainly high tones (4,000, 8,000) in one case (4 per cent.). Case No. III.

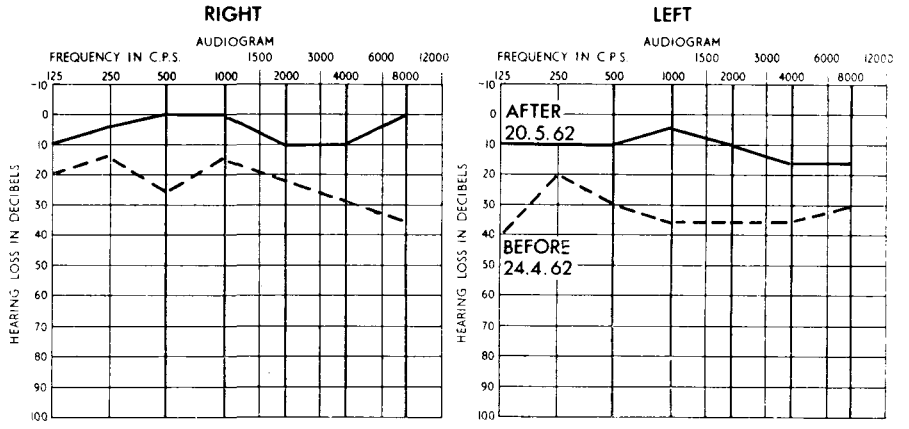
Improvement of 10–25 db. through the scale (more in high tones 4,000, 8,000) in one case (4 per cent.). Case No. IV.



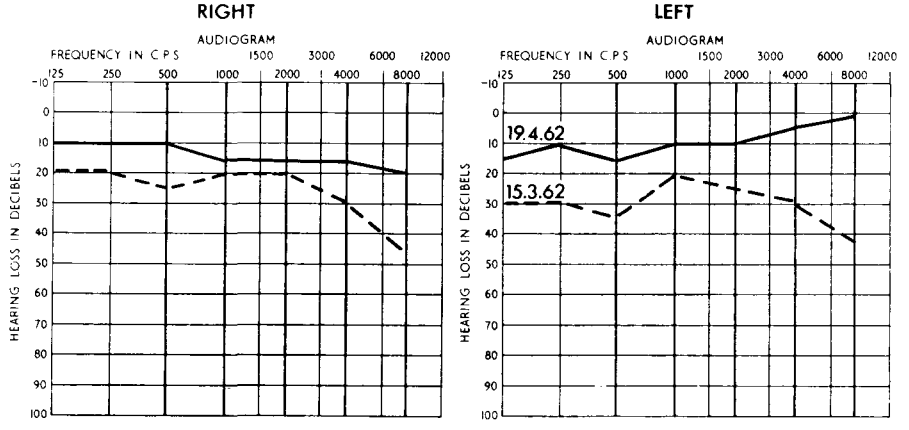
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Case No. I. S.A.H. ♂ 24 y.



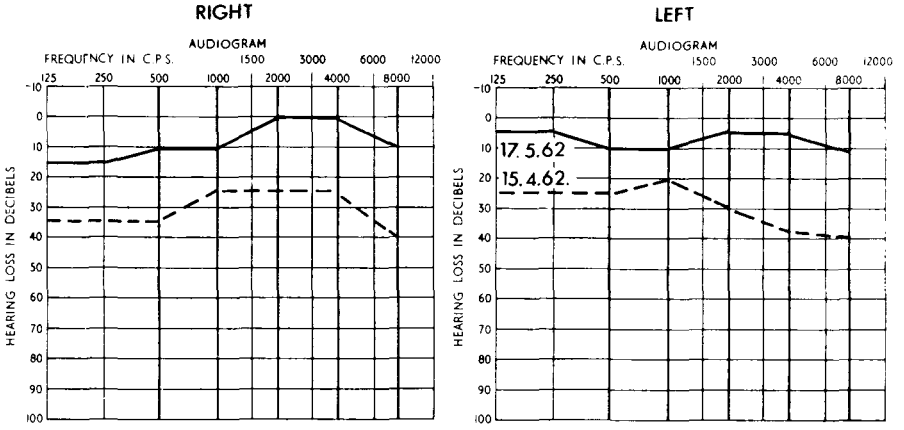

Case No. II. F.S. ♂ 30 y.




Case No. III. A.M.S. ♂ 27 y.



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Case No. IV. A.L.A.G. ♂ 29 y.

FIGURE.

Four examples of audiograms of cases before and after treatment.

Tinnitus was improved according to the patient's own assessment in three cases out of five. But they all stated that the improvement was not marked. The tinnitus did not disappear in any case.

Vertigo improved only in one single case. It is worth stating that among the cases who showed improvement by the audiogram, only two cases admitted improvement of hearing to a remarkable degree. The other three denied any change.

No marked change in the caloric test results could be obtained in any of the 25 cases after treatment.

## Comment

It appears evident in the survey already done that affection of the organ of hearing bears a relationship to pellagra which is a poly-deficiency disease of the vitamin B factors, especially nicotinic acid. We found perceptive deafness in about 30 per cent. of the cases. Neurologically normal cases showed normal hearing threshold. Vertigo and tinnitus occurred in 16 and 20 per cent. of the cases respectively. Regarding the effect of treatment with nicotinic acid on the other hand it seems that treatment of the deficiency state present bears a positive relation to improvement in hearing in the cases described. The effect of nicotinic acid on hearing in these cases is most probably due to its pharmacological action as a vitamin not as a vasodilator agent; since almost the same proportion showed improvement in the cases treated with its amide. Selfridge relates improvement in hearing in his cases to both the pharmacological and pharmacodynamic action of nicotinic acid.

As regards the vestibular apparatus, it was found that it is more stable to the deficiency state present than the cochlea. Nearly 20 cases



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showed normal caloric response. The effect of treatment by nicotinic acid or its amide seemed to have no demonstrable effect on the caloric response of the cases examined after being treated.

## REFERENCES


BIETTI, A. (1901) *Klin. Mbl. Augenheilk.*, **39**, 337. Quoted by Elwan.
CALDERINI, L. (1847). Statistiche sulla Pellagra. Milan. Quoted by Elwan.
CAWTHORNE, T. E. (1947) *Ann. Otol. (St. Louis)*, **56**, 18.
———, FITZGERALD, G., and HALLPIKE, C. S. (1942) *Brain*, **65**, 161.
CHURCH, C. F. (1933) *Proc. Soc. exp. Biol. (N.Y.)*, **30**, 1158.
CODY, C. C. (1932) *Arch. Otolaryng.*, **156**, 661.
COVELL, W. P. (1937) *Ann. Otol. (St. Louis)*, **46**, 895.
DENNY-BROWN, D. E. (1947) *Medicine, Baltimore*, **26**, 41. Quoted by Robin.
——— (1949) *New Engl. J. Med.*, **241**, 144.
ELWAN, O. H. (1959) Neuro Psychiatric Studies in Pellagrins in Egypt. Thesis.
FOUTS, P. J., HELMER, O. M., LEPKOVSKY, S., and JUKES, T. H. (1937) *Proc. Soc. exp. Biol. (N.Y.)*, **37**, 405.
FROSTIG, J. P., and SPIES, T. D. (1940) *Amer. J. med. Sci.*, **199**, 268.
MOUSA, A. H. (1960) Tropical Medicine and Infectious Diseases. Cairo.
ONO, T. (1928) *Trans. Jap. path. Soc.*, **18**, 172. Quoted by Selfridge (1939c).
DE RAADT, O. L. E. (1947) *Acta oto-laryng. (Stockh.)*, **35**, 231.
ROBERTS, S. R. (1912) Pellagra. London. Quoted by Elwan.
ROBIN, I. G. (1952) Toxic deafness. *In* Scott-Brown, W. G., Diseases of the Ear, Nose and Throat, **2**, 289.
SANDWITH, F. M. (1898) *Brit. J. Derm.*, **10**, 395.
SELFRIDGE, G. (1937) *Ann. Otol. (St. Louis)*, **46**, 93.
——— (1939a) *Ann. Otol. (St. Louis)*, **48**, 39.
——— (1939b) *Ann. Otol. (St. Louis)*, **48**, 419.
——— (1939c) *Ann. Otol. (St. Louis)*, **48**, 608.
——— (1940) *Ann. Otol. (St. Louis)*, **49**, 674.
SPIES, T. D. (1938) *Lancet*, **1**, 252.
———, BEAN, W. B., and STONE, R. E. (1938) *J. Amer. med. Ass.*, **111**, 584.



8 Gâmhâria Street,
Cairo,
Egypt




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