hypertrophy of the tonsils and adenoids might be avoided. It can be used for children awaiting tonsillectomy as in this trial, for at the present time most hospital waiting-lists are long and there is often a delay of over a year before the operation is carried out. Some doctors and many parents believe that once the tonsils have been pronounced "infected" they will remain so. Indeed, children are often referred to the ear, nose, and throat surgeon after their first attack of tonsillitis in the belief that further attacks can be confidently expected in the future and will be avoided if the tonsils are removed. The length of hospital waiting-lists for tonsillectomy encourages this practice. It is felt that the judicious employment of chemoprophylaxis and the prompt treatment of severe acute infections with penicillin will bring about a considerable reduction in the number of children requiring removal of their tonsils and adenoids and avoid much illness and loss of time from school.

Summary

Forty-eight children awaiting tonsillectomy were observed for eight winter months. Each child received either prophylactic sulphadimidine or calcium tablets. Half began with 0.5 g. of sulphadimidine daily, while the other half received a calcium lactate tablet identical in taste and appearance. The groups were changed after four months. The trial was conducted on the double blind principle.

Twenty-eight children fared better on sulphadimidine, 3 were worse, and in 17 there was no appreciable difference. During the period on sulphadimidine 25 acute infections were recorded, absence from school totalled 30 weeks, and the family doctor was called to treat 25 illnesses. The corresponding figures for the period on calcium tablets were 60 acute infections, 80 weeks lost from school, and 41 illnesses requiring treatment by the doctor.

Tonsillar hypertrophy and cervical adenitis were favourably influenced by chemoprophylaxis.

Chemoprophylaxis did not seem to affect nasal obstruction or reduce the incidence of the common cold.

Reasons for using chemoprophylaxis in preference to penicillin prophylaxis are discussed.

It is considered that chemoprophylaxis is worth a trial as an alternative to tonsillectomy in children subject to recurrent infections of the upper respiratory tract and, if instituted promptly, would result in a reduction of the number requiring this operation.

I am indebted to Professor R. S. Illingworth, who suggested the need for an investigation along these lines, and to Professor G. M. Wilson, who gave valuable advice on the planning of the trial and presentation of the results. I thank Mr. H. S. Sharp for kindly allowing these observations to be made on his patients; Dr. R. E. Bonham-Carter and Professor A. Moncrieff for encouragement and advice; Dr. C. Carter for advice on the statistics; the family doctors who gave information about their patients; and Imperial Chemical (Pharmaceuticals) Ltd. for supplying the tablets and for their successful efforts to make them palatable and acceptable to the children.

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SENSORY RADICULAR NEUROPATHY IN A DEAF CHILD

BY

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A number of cases have been described by various authors under different titles which may well be variants on one syndrome—characterized by painless ulcers of the feet, arthropathy, and deafness. The early literature includes four cases in one family described by Brüns (1903) as "syringomyélie lombosacrée familiale probable." Göbell and Runge (1914) reported a series of nine cases of "lumbar syringomyelia" without deafness in a single family covering two generations. Guillain and Thévenard (1929) published a report of a similar family. Hicks (1922) reported that 34 members in one family had perforating ulcers of the feet; and deafness was present in 10. In 1949 Murray Jackson reported 26 cases of "familial lumbo-sacral syringomyelia" in one family covering four generations. He noted that in this family there was an associated spina bifida occulta.

In 1940 a symposium of cases was described under the title of "L'acropathie ulcère-mutilante familiale" by Thévenard, Van Bogaert, André, and Goethals-Borin, with further post-mortem findings. The authors concluded that the cases described were examples of sensory radicular neuropathy.

The following case falls into this clinical group; it is of interest because the disease appeared at an unusually early age.

Case History

The patient was born on February 20, 1947. He was the second of three children of healthy parents; both siblings were healthy. There was no history of perforating ulcers of the feet or of deafness in the family (which has been traced back as far as the great-grandparents). The patient and his father and elder sister are left-handed.

The mother was in poor general health during pregnancy. Labour was rapid and the child was rather shocked at birth, but soon recovered and thereafter made satisfactory progress. At the age of 15 months, while he was crawling round the garden, he cut his knee badly and yet did not cry. His parents had been aware, since then, that he did not feel pain as acutely as their other children.

At 2½ years he could walk and feed himself, but made no attempt to talk and took no notice when spoken to. He was certified as an imbecile and committed to an institution.

In November, 1950 (aged 3½ years), he burnt his right forearm by putting it into boiling water. A year later he received a third-degree burn on the left thigh from sitting on a too-hot bedpan. These injuries seemed to be painless. In December, 1950, he developed a painless indolent ulcer on the plantar aspect of the left great toe, which took four months to heal. A few months later it broke down again despite rest in bed. The toe was therefore amputated. In September, 1953 the neighbouring toe developed an ulcer. This healed when he was confined to bed, but broke down as soon as he was allowed to walk about.

Findings

On examination he was a friendly little boy, of normal physical development. The occipitofrontal circumference of the skull was 20 in. (50.8 cm.). He was of normal intelligence and left-handed. The cranial nerves were normal in all respects except for the eighth nerve.

Eighth Nerve Function.—Dr. D. S. Hallpike, in his report, stated: "Nothing abnormal was to be seen on examination of his ears, nose, and throat. Cochlear function: he responded briskly to loud noises sounded without warning behind him. We were able to carry out pure-tone audiometry by means of the 'peep-show' procedure (Fig. 1). This shows an unusual type of hearing loss, chiefly affecting the hearing for the lower tones. Vestibular function: there was no spontaneous nystagmus. Optokinetic nystagmus was normal. With the caloric tests, no responses were obtained from the left ear with stimuli of normal strength. Slightly reduced responses were obtained from the right labyrinth."

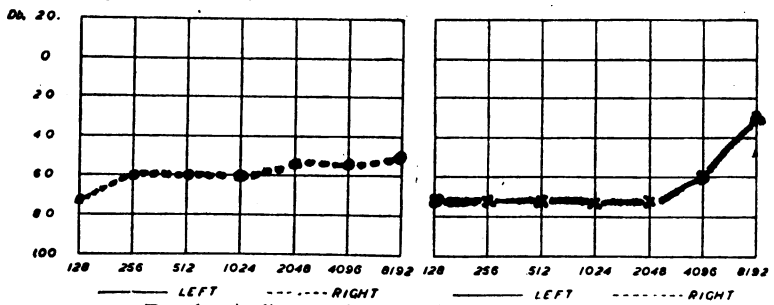

FIG. 1.—Audiogram (pure tone). November, 1954.

Motor.—Tone–power co-ordination of limbs normal. No wasting or fasciculation. He could run nimbly.

Reflexes.—Deep: Biceps- and triceps-jerks present; supinator absent in both arms; knee- and ankle-jerks absent in both legs. *Superficial:* Abdominal reflexes present; plantar responses absent.

Sensation.—Touch: Localized and probably normally perceived. *Proprioception:* Able to detect a change of position and give direction accurately with fingers and toes. *Pain:* When his attention is distracted, pin-prick is disregarded over the periphery of the limbs. He begins to resent pin-prick at an ill-defined level in upper third of thigh and just proximal to wrist (Fig. 2). Deep pain is also absent, and he does not object to forceful squeezing behind the tendo Achillis. Temperature is impaired over a similar area.

Axon Reflex.—Normal triple response to scratch over trunk and upper arms, with well-marked weal and flare. No response over area of sensory impairment.

Autonomic.—Normal sweating produced with heat, with rather profuse sweating of both feet (as judged by colour change in "quinizarine" powder). *Reflexes:* Normal pilomotor response; anal reflex normal; oculo-cardiac and carotid sinus reflexes normal; vasomotor responses normal.

Trophic Changes.—Several scars on both hands and legs. Skin of fingers coarse; skin of feet also thickened. No trophic changes in nails.

The second toe of the left foot was severely ulcerated on admission and the terminal phalanx was gangrenous (Fig. 3). Acute cellulitis developed; this was quite painless. When no one was watching he would get out of bed and join the children at a game of football.

Special Investigations.—E.C.G., normal record with sinus arrhythmia. E.E.G., normal. E.M.G.: The left gastrocnemius was examined on March 16, 1955, and both sides on April 1, 1955, the medial popliteal nerve being stimulated with brief shocks at 1 per second and the shock gradually reduced until no E.M.G. was recorded (with surface electrodes) from the gastrocnemius. On each occasion there was quite certainly no delayed wave with a threshold below that of the motor fibres stimulated directly. There is thus evidence of absence of low-threshold afferent fibres (believed to be A-fibres by Hoffmann and Magladery). Blood pyruvate metabolism, normal. W.R. and Kahn test, negative. *X*-ray examination of skull, normal. *X*-ray examination of left foot: Thickening of shaft of second tarsal and fragmentation of epiphysis. He had a spina bifida occulta of L5. *Circulation:* Limbs warm, peripheral pulses normal, and vascular responses to heating normal.

Nerve Biopsy.—The interdigital nerve of the third toe of the left foot was taken for histological examination. Report

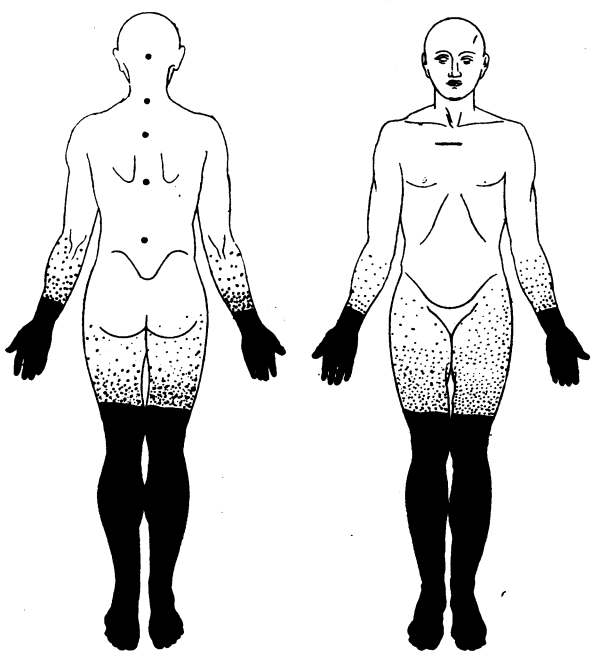

FIG. 2.—Impaired sensation for pain and temperature.

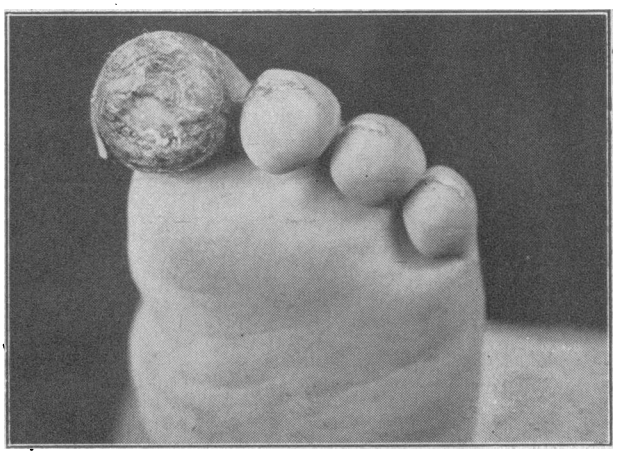

FIG 3.—Photograph of sole of left foot.

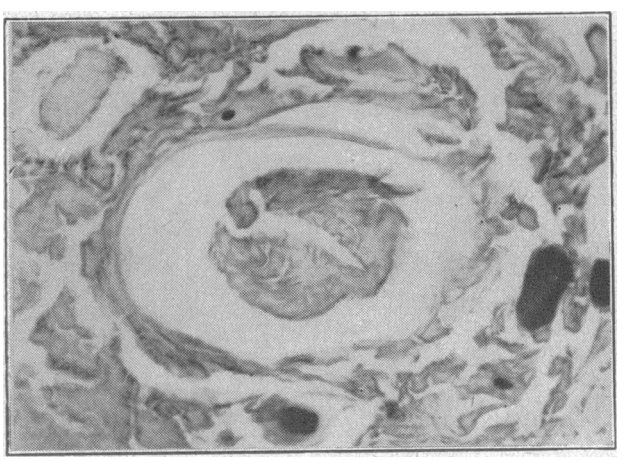

FIG. 4.—Section of interdigital nerve.

by Dr. W. Blackwood: "The material was fixed in osmic acid. It was found to consist of fibro-fatty and vascular tissue in which were at least three small nerve bundles. The space between the bundle and the perineurium was unusually large, as if the nerve had shrunk. Endoneurial fibrosis was not apparent. Tissue recognizable as myelin was not seen, although surrounding fat stained well. There was thus no evidence of myelination and positive evidence of shrinkage of the nerve bundles." (Fig. 4.)

Clinical Features of Cases Previously Reported

The published cases have certain features in common: impaired sensation for pain and temperature, trophic lesions of the feet, and, in some cases, nerve deafness.

The *sensory loss* appears first, and is most pronounced in the lower limbs; pain and temperature are impaired at first, and touch and proprioception remain intact, although these modalities may be affected eventually. The painless ulcerating lesions occur initially on the plantar aspect of the feet, especially on the big toe. Bony changes develop, with osteoporosis, and there may be arthropathy, especially of the metatarso-phalangeal joint. Ulceration may be unilateral at the onset, but becomes bilateral in over three-quarters of the recorded cases. Trauma plays a very important part, and with rest in bed the ulcers usually heal well.

In about half the cases trophic lesions do eventually occur in the fingers, often many years after they have occurred in the feet.

Vasomotor and Sweat.—There is no disturbance of blood supply. Sweating is normal, although hyperhidrosis of the feet has been reported in a few cases (Thévenard, 1953).

Paraesthesiae.—In the family reported by Hicks (1922), 10 cases had "lightning pains" of a "tabetic type," but this has not been found in other cases. The *deep reflexes* are absent or depressed early in the disease, the ankle- and knee-jerks being lost first. The loss is usually bilateral and symmetrical, but in 3 cases out of 48 (Thévenard, 1953) the areflexia and ulceration were unilateral.

Motor power is normal; the electrical reaction of muscles is normal or very slightly altered. Impairment of the sphincter control is rare.

Deafness.—In the family studied by Hicks there was severe bilateral nerve deafness, which was progressive. In some families there is no deafness.

The occurrence of *associated developmental abnormalities* has been noted, and a fairly high percentage of these cases have a spina bifida occulta.

Heredo-familial.—The majority of the cases have a family history of the condition, but sporadic cases have been recorded.

Course.—The initial symptom is usually painless ulcers of the feet. The age of first occurrence varies; most commonly it is between 15 and 30 years. The nerve deafness usually appears some years later, and progresses slowly to severe disability.

Pathological Changes and Mechanism of Symptomatology

The first case to reach necropsy was described by Denny-Brown in 1951. He showed that there was no syringomyelia or myelodysplasia. The essential lesion was a degeneration of the posterior root ganglion, and the most profound changes were in the lowest lumbar and first and second sacral ganglia. The maximum loss was in the smaller ganglion cells. The peripheral nerves and nerve roots showed a considerable loss of nerve fibres, and a patchy distribution of the loss was noticeable. The loss was more pronounced distally, and chiefly affected the small fibres. These small fibres and ganglion cells are supposed to record pain, and this may in part account for the dissociated sensory loss.

Deafness.—There was a reduction in the number of cells of Scarpa's ganglion and the cells of the spiral ganglion; also, some of the ciliated cells of the organ of Corti showed some degeneration. The atrophy of the cochlea and vestibular ganglia is similar to the process in the posterior root ganglion.

Interpretation of Eighth Nerve Ganglia Degeneration: Embryological Development

Before the neural groove is closed to form the neural tube, a ridge of ectodermal cells, the ganglion ridge or neural crest, appears along the margin of each neural fold. Opposite the primitive segments the cells proliferate rapidly to form a series of oval-shaped masses which migrate a short distance in a lateral and ventral direction. From the ventral part a small portion is detached to form sympathochromaffin cells, while the remainder form the spinal ganglia. The cells of the ganglia form spindles; the ventral processes grow into the neural tube to form the posterior root. The original bipolar form is retained in the retina and in the ganglia of the auditory nerve.

As the lips of the neural groove fuse in the region of the hindbrain, a ganglion crest is formed which is homologous with the neural crest of the spinal cord; from this is formed the ganglia of the vagus, glosso-pharyngeal, auditory, facial, and trigeminal nerves; these migrate, to lie on the ventrilateral aspect of the hindbrain.

Clinical Findings in Present Case

1. *Sensory and Reflex Disorder.*—This child has normal motor power. He has normal sweating and other autonomic reflexes. There is impaired sense of pain and temperature over the legs; vibration, position, and touch sensibility are probably intact. The axon reflex is normal over the trunk, but is absent over the area of sensory loss. These clinical findings are consistent with a lesion involving the posterior root ganglia of the lumbar, sacral, and lowest cervical regions. But all the cells in the affected ganglia cannot be equally involved, for on clinical testing there is dissociated sensory loss. In the interdigital nerve there are no myelinated fibres left, indicating that the small ganglion cells serving pain and temperature are very severely affected.

2. The *otological disorders* are of especial interest. There is a severe organic disease of the eighth-nerve system, with an unusual type of hearing loss for the lower tones, and with reduced labyrinthine responses. These findings indicate impairment of nerve conduction and of labyrinthine functions. The type of hearing loss is compatible with degeneration of the organ of Corti. They are consistent with a lesion in the ganglia of the cochlea nerve (spiral ganglion) and in the ganglion of the vestibular nerve (Scarpa's ganglion), and possibly the organ of Corti too.

Some Points in Differential Diagnosis

It is important to differentiate these cases from "congenital indifference to pain." These latter also develop arthropathy and trophic lesions of the feet, but in these cases the lesion is central, the deep reflexes are normal, the axon reflex and sympathetic reflexes are intact. The indifference to pain is generalized. There may be associated difficulties in speech and in the use of symbols suggesting a lesion in the "parietal lobe."

Myelodysplasia with spina bifida occulta can produce sensory loss, trophic lesions, and loss of deep reflexes, but if extensive enough to give this degree of sensory involvement one would anticipate motor and sympathetic components.

Morvan (1883, 1889) described a group of cases, unfortunately not confirmed by adequate necropsy studies, but forming a clinical syndrome clearly differing from sensory neuropathy. The chief points of difference are that "Morvan's disease" chiefly affects the arms, there is muscular atrophy, and a patchy sensory loss; the deep reflexes may be preserved.

Comment

This single case is worth reporting because of the early age of onset of anaesthesia and trophic change; also the very early age of onset of deafness, which led to certification as a mental defective. The cases so far described occurred at a later age, usually between 20 and 30 years.

There is little doubt that the anatomical localization of the lesion in this case is in the posterior root ganglion and the ganglia of the eighth cranial nerve; but the pathogenesis is not clearly defined. The group of cases may well include several syndromes of differing aetiology with differing clinical courses. This child may eventually prove to have a progressive degenerative lesion, possibly secondary to an inborn error of enzyme metabolism, but the rate of progression would appear to be very slow; in fact, there is very little to suggest deterioration so far. Alternatively, this might be due to a fault in the development of the posterior root ganglion.

Summary

A case of sensory radicular neuropathy is described in a boy of 8 years, who has been so deaf from early infancy that he had never acquired speech. He had impaired pain sense at the age of 15 months. There is no family history of the condition. He presented with painless ulceration of the toes, symmetrical loss of deep reflexes, the axon reflex, and impaired sensation to pain and temperature over the periphery of the limbs: proprioception, touch, vasomotor responses, and sweating remaining intact. Histological examination of the peripheral sensory nerve showed demyelination.

This case is compared with cases previously reported and the mechanism of symptomatology briefly discussed.

I am greatly indebted to Dr. P. Sandifer for permission to publish this case, and I thank Dr. D. S. Hallpike for his report on the otological findings, Dr. W. Blackwood for his biopsy report, and Dr. J. Simpson for the electrical studies.

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Statistics recently issued by the Armed Forces Medical Library, Washington, the world's largest medical library, demonstrate the immense output of literature concerning medicine and related subjects. During the year ended June, 1955, the library acquired 14,000 books, 77,000 parts of journals, and 1,182 new journal titles; it lent 168,000 volumes, answered 10,310 reference questions, and compiled 405 bibliographies of some length. In response to 101,000 orders it filmed 1,640,000 pages, and it published in the *Current List of Medical Literature* 102,645 items from 1,560 journals regularly indexed. During the year an average of 216 persons were employed by the library and the running costs were $1.2 million.

HAEMOGLOBIN E IN BURMESE

TWO CASES OF HAEMOGLOBIN E DISEASE

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Besides normal adult haemoglobin (haemoglobin A) a number of genetically determined variants are known (S, C, D, E, G, H, and I), and there is evidence, more complete in some cases than in others, that seven of these forms (not H) are the products of allelic genes, heterozygotes having varying quantities of the two kinds of haemoglobin concerned. The distribution of these genes is governed by various factors: mutation rates, genetic drift, and natural selection. A balance may be reached between the selection rates for two or more genes especially if the heterozygotes are more viable than the homozygotes, when a state of balanced polymorphism will be reached. However, the most obvious factor in the present distribution is an anthropological one.

Haemoglobin S (sickle-cell haemoglobin) is found in African Negroes between the Sahara Desert and the River Zambesi and in their known descendants elsewhere, and also in some peoples of the Mediterranean area and in some Veddoids of India and Arabia. Haemoglobin C has so far been found in West Africa and in places where it may have been introduced by West African slaves. Haemoglobin E was first reported in one child whose father was of part Indian origin (Itano *et al.*, 1954; Sturgeon *et al.*, 1955), and it was simultaneously discovered in the Siamese (Chernoff *et al.*, 1954a). It has since been observed in Veddas (Graff *et al.*, 1954) from Ceylon and in Indonesia (Lie-Inju Luan Eng, 1955). We would like to report that we had recently the opportunity of examining a group of Burmese in this country. Among 80 young adults—78 of whom were unrelated—12 with haemoglobin E were discovered. Ten had both haemoglobin A and haemoglobin E and two were homozygotes.

Haemoglobin E Disease

To describe a person as homozygous for a gene responsible for an abnormal haemoglobin is not strictly permissible unless the diagnosis by electrophoresis has been confirmed by a family study. The thalassaemia gene causes suppression of haemoglobin A formation. In microdrepanocytic disease, a condition in which AS heterozygotes also carry the thalassaemia gene, formation of A can be suppressed to such an extent that laboratory diagnosis may not be able to distinguish between the resultant phenotype and that of S homozygotes, although the genotype will be AS in one and SS in the other. Thus two individuals were recently seen in the Gold Coast (Edington and Lehmann, 1955) who, on the basis of laboratory examinations, were at first assumed to be homozygous for S, but a subsequent family study revealed that they were in fact AS heterozygotes who were carrying a thalassaemia or thalassaemia-like gene. Allison (1955) has