# Amyotrophic Lateral Sclerosis Among Guamanians in California

**JOSE TORRES, *B.S.*, Bethesda, Maryland,**
**LORENZO L. G. IRIARTE, *M.P.H.*, Agana, Guam, and**
**LEONARD T. KURLAND, *M.D., Dr. P.H.*, Bethesda, Maryland**

• **Amyotrophic lateral sclerosis is known to be prevalent among the Chamorros or natives of Guam and the other Mariana Islands. In a survey of adult Chamorros who had been residing in California it was found that the prevalence was equally high among that group.**

**Guamanians residing in California were found to eat diets similar to those of other Californians and to be living in housing which was similar to that of the other California populations of the same income status. A few native articles of food which were received occasionally by some of the Guamanians were not believed to be of etiologic significance in ALS.**

**The data on the prevalence of ALS among the Guamanians in California suggested that change of environment from Guam to California does not prevent the disease in persons predisposed to it. The data support the view that ALS is due to a genetic mechanism.**

A STUDY WAS MADE of the comparative prevalence of amyotrophic lateral sclerosis among Guamanians residing in California and among those in Guam. (The amyotrophic lateral sclerosis syndrome and its essential components, progressive muscular atrophy and progressive bulbar palsy, are generally referred to as motor neuron or motor system diseases. The initials ALS will be used herein to refer to this disorder.)

ALS is about 100 times more prevalent among the Chamorro people of the Mariana Islands than in other populations of the world.[1,4] In Guam at any one time, one per cent of adult Guamanians are affected with the classical ALS syndrome whereas only one in 10,000 adults in the continental United States is so affected. About ten per cent of deaths in Guamanian adults are due to ALS in contrast to a death ratio of one per 1,000 adult population in other areas.[3] The clinical and pathological features of ALS in the Mariana Islands have been described in detail in other reports.[1,2]

In the Mariana Islands, of which Guam is a part, ALS is highly prevalent only among the Chamorros, the indigenous population of that island group. The prevalence is not increased either among the large number of United States ("stateside") military personnel on Guam or among the natives of the Caroline Islands who migrated to the Marianas many years ago.

Native legend has it that ALS has been prevalent in Guam for over one hundred years, and the Chamorros believe the disease to be familial. Familial aggregation of cases of ALS were, indeed, frequently encountered in earlier surveys.[6,2,7] It was not possible, however, to obtain complete and accurate pedigrees of families on Guam because of the uncertainty of some family relationships, the near absence of written records due to destruction of church and civil archives during the recent World War invasion, the lack of medical information about progenitors and the reticence of many in the population because of the stigma Chamorros frequently associate with this disorder. Although there is suggestive evidence that ALS on Guam is an inherited disorder, it has not been possible to obtain sufficiently accurate pedigrees to justify the conclusion that an endogenous etiological mechanism was responsible for the high incidence of the disease among the Chamorros.

It seemed that, if it could be shown that ALS continued to be highly prevalent among Guamanians residing outside the Mariana Islands, this would be further evidence that heredity and not environment played the more significant etiologic role in this disorder.

The Chamorros today are a heterogeneous mixture of the original settlers of the islands* with Spanish, Filipino and other racial strains added. Today, they number about 38,000, about 35,000 of whom reside in Guam, about 2,000 in the other Mariana Islands and about 1,000 in the continental United States.

The exact number of Guamanians living in the United States is unknown since, as United States

Medical Aide, Laboratory of Neuroanatomical Sciences, National Institutes of Health, Public Health Service, U. S. Department of Health, Education and Welfare, Bethesda 14, Maryland (Torres); Department of Medical Services, Government of Guam, Agana, Guam (Iriarte); Chief, Epidemiology Branch, National Institutes of Health, Bethesda 14, Maryland (Kurland).

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*The origin of the indigenous population of Guam and the other Mariana Islands is uncertain. It is believed that the island was first inhabited about 2,000 years ago by seafarers from Malaya or Indonesia.

citizens, they may freely migrate to and from the territory of Guam. However, it is estimated that about 250 families now reside in the continental United States and that about 150 of these families are in California. A few Guamanians are said to have settled in California after their arrival on whaling ships in the latter part of the 19th century. A few dozen families are believed to have settled in the continental United States before 1940, and the remainder after the end of World War II. The greatest influx has occurred since 1950. In most instances, young men who enlisted in the military forces before and after World War II have, upon assignment to California, settled there and brought over fiancees or wives and children at a later date.

## METHOD OF STUDY

In the present study carried out during the summers of 1955 and 1956 attempt was made to locate and interview all adult Chamorros residing in California. Persons with history of weakness, spasticity, dysarthria or other suspicious neurological conditions were examined for evidence of ALS.

A roster of Chamorros residing in California was developed with the aid of the members of the California Sons and Daughters of Guam Club. All persons who were interviewed were asked about all their Chamorro acquaintances.

The following information was sought for each Guamanian interviewed: Place and date of birth; length of residence in California; dates and duration of return visits to Guam, if any; nature and type of the present diet; type of food or other items, if any, received from Guam.

Special attention was given to determining whether the California group proportionately represented the population from all the villages on Guam, since earlier studies indicated that the disease is more prevalent in the southern villages of the island than in others. The studies on Guam also suggested that the ALS incidence rates are higher in the lower income families. However, it is uncertain whether the attendant impoverishment was related to the cause rather than the effect on wage-earning capacity of the disease in parents or grandparents who might have been affected in previous generations.

An evaluation of the economic status of the Chamorros interviewed in California was also attempted. Since it was not feasible to make a detailed inquiry, the interviewers resorted to a cursory observation of the dwellings, furnishings, sanitation and other physical evidence of the relative state of poverty or wealth.

Attempt was made to obtain a detailed family history with special emphasis on occurrence of amyotrophic lateral sclerosis. Since the disorder carries some degree of stigma in Guam, it was not surprising that some of the persons interviewed denied any knowledge of the disease, in spite of the fact that siblings or parents who had been observed in Guam had succumbed to the disease. A few persons would not assent to interview. In view of these circumstances, the data on family history cannot be considered reliable for the group as a whole.

**TABLE 1.—*Residence in California of Guamanians Interviewed in Survey***

| | Male | Female | Total |
|---|---|---|---|
| San Diego County area | 46 | 48 | 94 |
| San Francisco Bay area | 27 | 26 | 53 |
| Los Angeles County area | 10 | 8 | 18 |
| Total | 83 | 82 | 165 |

## RESULTS

One hundred and sixty-five adults, 83 men and 82 women, were interviewed. Of this group, 154 replied to all inquiries.

Sixty-six or 43 per cent of the total were under 35 years of age. Since ALS infrequently occurs before age 35, a substantial proportion of the group was in the lower risk age bracket.

For the entire group, the average period of residence in California was 7.4 years. At least 80 per cent had resided in the continental United States for less than ten years. Twelve per cent had been in California for 15 to 25 years and two per cent for more than 25 years.

The Guamanian families are found in many communities of California but they tend to be concentrated around the San Diego Bay area, the San Francisco Bay area and in Los Angeles County (Table 1). Many of the men were still in the Navy and their families resided in Navy housing facilities. Others settled in the Bay Area or San Diego County area after discharge or retirement from the Navy.

Most of the subjects interviewed had been residents of the northern villages on Guam. However, every Guamanian village was represented in the population interviewed.

It was the investigators' impression that housing, sanitation and diet of the Guamanian families interviewed were similar to those of the non-Guamanians in the same area. A few admitted receiving Guamanian articles, such as manahag (a small salted fish), achote (a coloring substance for rice) and betel nut. These substances were not incriminated as causative factors in the Guam studies.

Ten of the subjects interviewed said that other members of the family had died of ALS. (That this is probably a minimal figure may be assumed for reasons previously noted.)

Two men in whom ALS was suspected were found among the 165 subjects interviewed.

CASE 1. A 41-year-old Guamanian, a steward's mate in the U. S. Navy, was first seen at the sick bay of the U. S. Naval Auxiliary Air Station, El Centro, California, in December, 1954. At that time, he complained of painless weakness in the left hand which had started approximately four months previously. Upon physical examination at that time it was noted that there was mild weakness and atrophy of the left hand with weakness of the individual muscles of extension, flexion and abduction and adduction of the thumb. No pathologic reflexes were evoked. In routine laboratory studies and chest x-ray examination no abnormalities were observed. The blood pressure was 142/102 mm. of mercury.

No specific treatment was given. The patient was returned to duty a week later.

A year and a half later the patient was admitted to the U. S. Naval Hospital, San Diego, with symptoms of advanced ALS. At that time he complained of some nasal regurgitation of fluids. Pronounced atrophy of the interossei muscles, bilaterally, with concomitant weakness of the hands was observed. Atrophy and muscle fasciculations were noted about the shoulder girdle as well as in the tongue. There was decided weakness of all movements of the left ankle. The deep tendon reflexes were exaggerated throughout, except for the left ankle jerk, which could not be elicited. The sign of Babinski was present bilaterally. Results of routine laboratory studies and electroencephalograms were all within normal limits.

On examination two months later, other evidence of bulbar and pseudobulbar involvement was noted. Moderate dysarthria and dysphonia were present, as well as a sucking reflex and the nasal regurgitation previously mentioned. The patient was still able to walk about, but only with assistance.

The patient was the youngest of three siblings, the older two living and well. Both parents were about age 60 years and in good health. One first cousin in Guam had advanced ALS.

The patient had enlisted in the U. S. Navy in 1938 when he was 23 years of age, had come to the United States the same year and had been in this country or aboard ship ever since, except for a two-year period between 1948 and 1950 when he was stationed on Guam.

CASE 2. The patient was a 38-year-old laborer who had resided in California without interruption since 1940. An aunt had recently died of ALS in Guam. The patient had noted slowly increasing painless atrophy of the thenar and dorsal interossei muscles of both hands over the preceding few months. He had no other complaints. In addition to the atrophy and weakness of intrinsic muscles of the hands, there was weakness of the left deltoid muscle. Fasciculations were present in the muscles of the left shoulder girdle, right triceps and occasionally in the right calf muscles. The left bicep and brachioradial reflexes were hyperactive as compared to those reflexes on the right side. Coordination, sensory examination, intellect and bladder sphincter control were normal. There was no discomfort on rotation, hyperextension or hyperflexion of the head on the neck. The onset of symptoms in this patient was similar to that in scores of ALS patients observed in Guam, and although a definite diagnosis could not be made so soon after symptoms were first noted, the diagnosis of amyotrophic lateral sclerosis was strongly suspected.

If both the cases described were cases of ALS, two of 165 (1.2 per cent) of the adult Guamanians examined in this study were affected. As was noted earlier, this is about the same as the prevalence among adults on Guam or about 100 times that expected in similar samples of the indigenous population of California.*

In addition to the patients observed in the surveyed group, the investigators learned of five other patients among the small population of Guamanians who had resided in California in previous years.

The following experience was described by an elderly Guamanian who had retired in California and who was interviewed in the course of the present study:

As a young seaman, he said, he had visited California on many occasions. In 1910, he was asked by friends in Guam to visit two brothers who had arrived from Guam about 1885 and had settled in San Francisco. In 1908 progressive painless paralysis developed in one of the brothers, and the following year the other brother also became affected. Both patients were about 50 years of age.

The narrator was unable to recall the names of the brothers but his meeting with these two men was an otherwise unforgettable experience. He described the typical wasting of the hands, dysarthria, dysphagia and the spastic gait he had observed. Neither brother had complained of any pain and both were alert and responsive. The brother with advanced disease died the following year; the other, about a year later.

Two other cases came to the attention of the investigators in the present study from the rosters of ALS patients who were observed in U. S. Naval Hospitals in California between 1947 and 1953.

The first patient was born in Guam in 1910, enlisted in the Navy and was assigned to California in 1941. In November, 1947, he noted weakness and muscle twitchings in the lower and then the upper extremities. A diagnosis of ALS was made the following year and the patient returned to Guam. He had a typical progressive course with both upper neuron and lower motor neuron involvement. He

*The probability of finding a random sample of 165 non-Chamorro adults in California in which two are affected with ALS, and if the true prevalence is one in 10,000, is less than .002.

remained at the U. S. Navy Hospital on Guam with a diagnosis of advanced ALS and died in April, 1950.

The second patient was born in Guam in 1921 and enlisted in the U. S. Navy before World War II. He resided in California when he was not aboard ship. In 1951, weakness and wasting in the extremities developed. The patient had a typical progressive course and died 30 months after onset at the Veterans Administration Hospital in Los Angeles. At necropsy it was noted that the immediate cause of death was bronchopneumonia. Pronounced atrophy of the skeletal muscles of the extremities was observed. Upon examination of the central nervous system it was noted that there was degeneration of neurons in the anterior horns of the spinal cord and their analogues in the medulla. Betz cells in the motor cortex were degenerating or absent and were replaced by neuroglia. In the corticospinal tracts there was demyelination at all levels. The diagnosis was amyotrophic lateral sclerosis.

The investigators heard of one middle-aged female patient who had arrived in California about 1946. A few years later, a progressive paralytic disease developed and the patient was said to have died of ALS about 1952. However, she could not be identified well enough to lead to a clinical record.

The incidence of ALS, which is known to be high among the Chamorro population of Guam, appears to be equally high among the Guamanians who emigrated to California during the past few decades. This suggests that a change of environment does not prevent motor system disease among those who may be predisposed.

The results of the present study support the view presented in other reports[3,7] that the ALS which occurs among Guamanians is owing to a genetic mechanism rather than to one which develops only during residence in the Mariana Islands.

All the adults interviewed or examined in the present study had been born on Guam. None could be found who may have been the offspring of the very few Guamanians who emigrated to California 30 or more years ago.

Amyotrophic lateral sclerosis outside the Mariana Islands infrequently appears in familial aggregations. Careful family histories usually do not elicit other cases, but numerous pedigrees have been described in the United States and among at least eleven other nationalities.[3] It has been hypothesized that ALS is due to a genetic mechanism, not only in Guam but elsewhere in the United States and in the other countries as well.[3] It is believed that ALS is due to the inheritance of a dominant trait in which the penetrance is not complete.*

In a few of the patients with ALS on Guam who were part Chamorro and part American or Japanese, the patient's mother had also had amyotrophic lateral sclerosis. In other instances, the mother had not died of ALS although the disease may have been known to occur in her family. These instances also support the hypothesis of dominant inheritance with incomplete penetrance.

The data here reported would appear to emphasize the need to consider ALS as one of the diagnoses when a Chamorro or part-Chamorro has complaint of recent weakness or atrophy, even though the symptoms may be limited to one extremity or even part of the extremity.

On the other hand, it was also noted that several of the Guamanians who were interviewed had severe anxiety over the possibility that they might be developing ALS. For many of them a careful neurological examination with the reassuring statement that the results of examination were within normal limits and that the large majority (90 per cent) of Guamanians were not expected ever to develop this condition, gave relief from this distressing and useless state of anxiety. There is not as yet a means of predicting who will be affected and no way is known for preventing the relentless progress of this disorder even when it is seen in the early stages.

National Institute of Neurological Diseases and Blindness, Bethesda 14, Maryland (Kurland).

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*"Penetrance," as used here, refers to the percentage of individuals who, when they possess the gene, show any effect from it. Theoretically, if penetrance is complete and the gene is dominant, half of the offspring of an affected heterozygous individual will develop the trait. When an individual can transmit the gene responsible for the trait, yet shows no obvious manifestation of the disorder, it is said that the penetrance of the gene is incomplete.