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# The Star

RADIATING THE LIGHT OF TRUTH  
ON HANSEN'S DISEASE

the

Radiating the Light of Truth on Hansen's Disease

# STAR

C A R V I L L E, L O U I S I A N A

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STANLEY STEIN, 1899-1967.  
Founder-editor of The STAR.

*"There is still much to be done..."*

Unique Metabolic Properties of *M. Leprae*  
*K Prabhakaran* ..... 1

A Contemporary Visit to the Land of Myth  
*José Ramirez, Jr* ..... 2

**Gems from past issues**

Stanley Stein -- He Lived to Serve Others ..... 6

Ocular Leprosy  
*Margreet Hogeweg* ..... 7

Network of Support  
*Nicole H Holmes* ..... 11

Antioxidant Effect of Vitamin E in Patients  
on Antileprosy Chemotherapy  
*Vijayaraghavan R, Suribabu CS, Sekar B,*  
*Krishnamurthy KV, Narashimmamurty P, Panda PK,*  
*Oomen PK, Vinod Kumar CHD, Jeyarama E,*  
*Panneerselvam C\**..... 12

Dave's Desk----Carville Star (from the Forty and Eighter)  
*David Rabius* ..... 16

## Stanley Stein

**Founder - Editor, 1941 - 1967**

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The purpose of **The Star** is to: 1) Promote an educated public opinion of Hansen's disease, 2.) Furnish vocational rehabilitation for interested patients.

Views expressed in **The Star** are those of patients of the Gillis W. Long Hansen's Disease Center at Carville, Louisiana, except in the case of direct quotations or signed articles.

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### Editorial Policy On Terminology

**The Star** stands firm in its opposition to the use of the term "leprosy." We shall never abandon our campaign to secure general acceptance of "Hansen's disease." Nevertheless, the word "Leprosy" does appear in **The Star** under circumstances which we feel are unavoidable, namely: when signed articles are authored by someone who does not agree with us or when material discusses the disease prior to the introduction of the term "Hansen's disease." We dislike the word "leprosy" intensely, but we dislike the practice of censorship even more.

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# UNIQUE METABOLIC PROPERTIES OF *MYCOBACTERIUM LEPRAE*

\*K . Prabhakaran

Presented at The 16th International Congress in Salvador, Brazil

In spite of the multi-drug therapy introduced in the 1980s and the initiation of the leprosy elimination program proposed in 1986 to control the disease by year 2000, leprosy continues to be a serious public health problem in several endemic nations. Brazil along with India is among the few countries of the world in having a prevalence rate of 5 - 15 per 10,000 of the population. The incidence rate per 100,000 of India in 1995 was around 43; in 2000 it increased to 55; of Brazil it was about 21 in 1995, but increased to 24 in 2000. What will happen after 2005, when the elimination program has been rescheduled to end? Will the program be re-scheduled? What happens to the cases that relapse and those with multi-drug resistant bacteria?

*Mycobacterium leprae* has several characteristic properties not shared by other mycobacteria. I was the first to report the presence of the enzyme *o*-diphenoloxidase in *M. leprae*; no other mycobacteria, including *M. tuberculosis* and *M. lepraemurium* possess this enzyme activity. Genome sequencing in recent years has revealed the presence of a unique set of genes in *M. leprae*, which does not occur in *M. tuberculosis*. This observation accords with our finding of an unusual *o*-diphenoloxidase in the Hansen bacillus. On the other hand, *M. leprae* lacked several genes coding for biosynthetic enzymes, which were present in *M. tuberculosis*. Unlike free-living bacteria, *M. leprae* does not synthesize ATP; we have shown that it has a mechanism for transporting the energy-rich compound from the surrounding milieu. The deficiency of biosynthetic enzymes explains the inability of the Hansen bacillus for independent growth, that has thwarted attempts for over a century to culture the bacterium in chemically defined media. The finding contradicts the claim that *M. leprae* is a competent organism, a claim advanced by a few scientists in the field.

Properties of the *o*-diphenoloxidase of the Hansen bacillus distinguish it from a similar enzyme found in skin melanocytes. The bacterial enzyme converts 3,4-dihydroxy phenylalanine (dopa, both L- and D-isomers) as well as a variety of other diphenols to quinones in vitro; but the substrate specificity of the melanocyte enzyme is rather restricted to L-dopa; it is inactive towards D-dopa, dopamine, epinephrine, norepinephrine or other similar compounds.

The melanin pigment of the skin, eyes, hair and leptomeninges is derived from dopa. The *o*-diphenoloxidase of

melanocytes is completely inhibited by reducing agents like ascorbic acid (vitamin C) and glutathione; but reducing agents have no effect on the bacterial enzyme. In senile cataract, brown and black pigment accumulates in the lens, making it opaque. This is because the levels of ascorbic acid and glutathione decrease with age, activating *o*-diphenoloxidase. Older and middle aged people take note. Contrary to what ophthalmologists say, you can prevent cataract development by consuming vitamin C.

In a culture of melanocytes, granules of melanin pigment can be seen to accumulate. When a suspension of viable Hansen bacilli was added to such a culture, no pigment formation occurred; heated bacteria had no effect. Melanocytes hydroxylate tyrosine to generate trace amounts of dopa; if the bacteria divert the substrate for its own metabolism, no melanin formation would occur. This explains hypo-pigmentation of skin lesions in leprosy.

When dopa is added a purified suspension of viable *M. leprae*, color development due to conversion of the substrate to quinone can be observed within 30 min; heat-killed bacteria do not show the activity. The reaction mixture can be centrifuged and spectrum of the supernatant fraction measured for a quantitative assay. This can serve as an identification test. In all experiments, run a control with heated bacteria; otherwise, auto-oxidation of the substrate may be mistaken for positive activity.

Why does *M. leprae* invade the Schwann cells? The answer lies in the embryonic origin of these cells. Just like melanocytes, Schwann cells, as also the adrenal medulla, originate from the neural crest, and contain the enzyme tyrosine hydroxylase which generates dopa, an essential metabolite for *M. leprae*. Normally, reducing agents in the Schwann cells prevent oxidation of the dopa to melanin; sometimes in disease conditions, pigmented Schannomas may result.

In the armadillo, we have found that the adrenal medulla that is also derived from the neural crest and generates dopa is a preferred site for early multiplication of *M. leprae*, even before skin lesions start appearing in the animal.

Contd on page 16

# A CONTEMPORARY VISIT TO THE LAND OF MYTH

by José Ramirez, Jr

**José and his wife Magdalena went on a two-week tour of Turkey and Greece to gather information on HD. Their visit brought honors, surprises and new information on how**

On January 31, 2000, the Leprosy Association of Turkey, in conjunction with the Ministry of Social Welfare, celebrated World Leprosy Day. The celebration, held at the University of Istanbul, was designed to bring attention to the unjust stigma usually associated with chronic diseases.

The one-day event was titled "Public and Social Support for Chronic Diseases" and was widely covered by the print and electronic media, including CNN. A panel, led by Dr. Türken Saylan, Director of Turkey's Leprosy Hospital and Professor at the University of Istanbul's Medical School addressed the special significance of World Leprosy Day and the debilitating effect on those affected by leprosy from a community ignorant about myths, and the reality related to Hansen's Disease(HD).

Prior to presentations by the panel of speakers, Dr. Saylan presented three "Etem Utku Medals" in memory of this famous leprologist from Turkey. The medals were presented to Esin Küntay, social worker for outstanding social research in the field of leprosy; Erman Atasoy of Novartis for the support of medical research; and José Ramirez, Jr, social worker from Houston, Texas, **IDEA's** (Integration, Dignity and Economic Advancement) USA Coordinator and Board member of **ALM** (American Leprosy Mission). I received the medal for "outstanding international advocacy work in the field of leprosy".

I was suprised and honored with this unique recognition. When Dr Saylan asked me to address the audience, I recalled my visit the previous day to the mosque with the world's best preserved mosaic work, now known as Kariye Museum. The museum's ceilings depict many scenes described in the Bible. One area has the "Wall of Healing", with portrayals of Jesus healing various persons. It is believed that one of the damaged mosaic showed the "healing of a leper", thus my remarks referenced this famous Mosque.

"With today's availability of MDT" ,(multidrug therapy) I said, "physical healing can occur within a very short period of time. But it is the emotional healing that requires on-going advocacy work and education." I congratulated the various disability groups represented at the event and promised to continue honoring the memory of Etem Utku.

Dr Saylan, who has devoted most of her adult life as a volunteer, physician and educator in the field of leprosy, served as moderator for the presentations that followed.

The first speaker, Hason Gemici, Minister of Social Welfare and counterpart to the USA's Secretary of Health and Human Services, complimented the movement to unify all groups with disabilities, forming a powerful force. With this in mind, he committed, on behalf of the Turkish government, to provide funding to train professionals on how to link the approximately 6 million persons with chronic disabilities to employment opportunities..

The second speaker, Dr Esin Küntay, Professor at the School of Social Work, discussed how stigma dramatically impacted the 2,500 persons with HD living in a country with 60 million people.

Next, Kemal Kilicdaroglu, Director of Turkey's Social Services stated that persons with chronic disabilities such as mental illness, mental retardation, celebral palsy and diabetes were eligible for small pensions.

Frank Öztimur, Assistant to Turkey's Prime Minister and Director of the Disabled Federation, emphasized the need to advocate for employment for all persons with disabilities and for making buildings accessible to persons in wheelchairs.

Erman Atasoy of Novartis indicated continued support to attack chronic illnesses. Dr Ilhan Satman of the Diabetes Association noted the devastating effects of ignorance about this disease equating it to no treatment at all. Finally, Ziya Celik, a resident at the Istanbul Leprosy Hospital, passionately described how his diagnosis not only resulted in forced hospitalization, but also forced unemployment as he was terminataed from his job as soon as his employer received word of his illness in 1968. He credited the support of Dr Saylan and her staff for his mental and physical recovery.

The World Leprosy Day celebration ended with a promise to continue the fight of ignorance.

The next day, two of Dr Saylan's most devoted followers, Dr. Ayse Yuskel (Professor at the School of Medicine) and Hatice Erdogan (Director of Nursing) served as my guides to the Leprosy Hospital. The two ladies are friends I had met previously in Spain and China at **IDEA** sponsored workshops.

The Hospital is located on a hill and was built at a time when this area was considered to be on the outskirts of

Istanbul, past the ancient walls of Constantinople. The hospital complex did not have fortress like walls, but visitors did have to pass a security gate. The facility, now with less than 40 residents, was in the middle of two other institutions. One was a large enclosed complex for the chronically mentally ill and the other an even larger facility with 20-foot walls, razor sharp barbed wire and armed sentries - "a military hospital for dangerous criminals." The hospital was on an island, surrounded not by water, but by other people traditionally ostracized by society.

The residents had different levels of disabilities and unlike many other hospitals throughout the world, this had a varied age group, ranging from the 20's to the 80's. I greeted each of my brothers and sisters with a hello or "Merhaba" and facial embrace on both cheeks.

There are two other hospitals throughout Turkey. However, the one in Istanbul is the only one with the facilities to provide ongoing therapy. It is also Turkey's center for making all of the special shoes worn by an aging population with disabled and ulcerated feet. Most of the work in making the shoes is expertly done by the residents.

The residents live in ward like facilities and five married couples live in apartments comprised of three 10 x 12 rooms - living room, kitchen and bedroom.

Ziya invited me to visit his small apartment, "my home" he said. Before entering, I removed my shoes in respect to his Muslim beliefs. He welcomed me in a traditional Muslim manner by splashing aromatic cologne on my hands in order to clean my nostrils and thus smell the beauty of his home. He also fed me rice pudding with cinnamon.

Ziya then showed me his wedding picture, and like me, married a woman without HD. Without understanding our words, we understood our unique culture and smiled about overcoming similar experiences filled with pain and ignorance. We bid our farewells in the same manner we had greeted each other - with a gentle rubbing of each other's cheeks.

The next day, my wife Magdalena and I and our good friends from Houston, Willie and Gloria Quintanilla, boarded a ship with plans to visit several islands before disembarking in Athens.

The next four days gave me additional insights into how history and present society have had similar views on people with leprosy. On the first day of our ride on the ship, we viewed a promotional video which focused on the different tours, including a visit to the ancient port city of Ephesus on the island of Kusadasi, and Spinalonga, the "last leper colony in Europe" on the island of Crete.

According to numerous historians and medical researchers,

leprosy arrived in the Aegean Sea through slaves transported by Alexander the Great, Romans and Crusaders. All three also transported the stigma and fear, thus places of isolation were identified in effort to contain the disease.

Our ship passed many of the islands previously used as "leper colonies".....the islands of Mt Athos, Samos and Leros, off the coast of Turkey. The "outcasts" were forced to live on their own as best they could, on abandoned fortresses or in monasteries as unpaid laborers. Greece also had "colonies" on a small cape on the northwest corner of the island of Rhodes and the better known Spinalonga off the coast of Crete.

The ship's first stop on the island of Kusadasi gave us the opportunity to visit the home where St. Mary, the mother of Jesus, lived after her son's crucifixion. This was an exhilarating sight until told by the tour guide that the fountain of St. Mary was said to be "healing water, except for lepers." The tour guide explained that because the disease was so feared even today by the locals, persons suspected of having leprosy would be barred from the fountain of St. Mary.

Ironically, I was wearing **IDEA's** "Quest for Dignity" cap (International tour of the HD Exhibit). During this walking tour, I was asked by a fellow tourist what it meant. When I explained the significance, she was aghast to hear that leprosy still existed, especially since all of the tours implied that this disease had been extinct for many years. This chance encounter with the pretty lady from California opened up opportunities for me to educate others in the group about HD.

The ancient port city of Ephesus was one of the most modern cities of its time, with a huge library, beautiful jewelry, a well stocked market, running water, public toilets, large stadiums and theaters, exquisite statues such as Nike the Goddess of Victory and a large hospital. In spite of its modern ambiance, the leaders of Ephesus still "refused to treat lepers" who were instead banished to one of the islands previously mentioned. Even though the "biblical leper" asked Jesus "if you will, please heal me," the populace of Ephesus were not accepting of this grossly misunderstood disease.

We left this beautiful community, shrouded in a cold rain, feeling both exhilaration in viewing a place we had previously seen only through our imagination, and also sadness because of the fear that has always followed the leprosy bacillus.

Our next stop was at a large island located farther south, Rhodes. Rhodes is commonly known for it's mink, the old fortress now known as "Old Town" and Lindos, the site of the temple of Athena, with over 250 steps which "lead to

the heavens." Lesser known to the tourist is the monastery used to "house lepers" in the past. Lesser known still is the small Bay of Hippocrates where the Father of Medicine used to go bathe and experiment with the plants growing in the area and used them for medicinal purposes.

One of the plants he reportedly experimented with was the fruit from the Karobe (sic) tree. The fruit, a long stem with beans or seeds inside, reminded me of a smaller version of the fruit from the mesquite tree, common throughout south Texas.

According to the tour guide, Hippocrates used the Karobe fruit to make tea to treat what is now known as diabetes, the locals ate the fleshy meat for its sugary content and jewelers used the seeds, resembling chocolate chips found in today's cookies to weigh fine gems.

The residents of "the colonies" knew that Hippocrates experimented with this fruit. The men who completed their medical studies bathed in Hippocrates' bay and drank tea made from the Karobe tree. Reportedly, "the outcasts" grew this tree on their usually barren islands, hoping and praying that it would be their miracle medicine to cure them of leprosy.

The next island on our tour was Crete, the largest island in the Aegean Sea. Crete is known for having had 8,000 years of myth. Our landing was on the city of Herakleion, surrounded by fortified stone walls built during Venetian rule, 1204-1669.

We chose to take a scenic tour of the coast, going to Aghios Nikolaos. This small community served as a springboard for the Venetians to take a short sea trip to the island of Spinalonga, an island so barren soil had to be transported in order to plant anything. Spinalonga reminded me of a much smaller version of Alcatraz. **The Star** published an article on Spinalonga written by Beryl Daryl of England in 1986.

The Venetians built a fortress and defended their occupation of Crete until ousted by the Turks. Eventually, the Cretan Republic passed a resolution to convert Spinalonga to a "leper colony" in 1903. Hundreds of people from throughout Greece eventually were "sentenced for life" to Spina longa and many of the "inmates" died of secondary infections due to a dearth of medical care.

Similar to most other "colonies" throughout the world, conditions were harsh and isolation from the rest of society forced the residents to form a federation in order to have a semblance of organization and community living. The end result was the creation of a system to complete essential tasks such as fishing, cooking, etc. A one-cell jail was built to enforce order and prevent civil disobedience.

During WW I and II, the island was not occupied by any troops. However, soldiers were assigned on opposite shores to prevent escape. The conditions were so bad during the Italian and later German occupations, that the residents of Spinalonga sent written pleas to the two dictatorships for humane treatment. When their pleas were ignored, many protested by going on a fast, resulting in death by starvation. The arrival of the Allies brought the availability of food, but the law of 1903 continued to be honored and thus social exclusion continued. In 1957, the government of Greece closed the facility and moved 28 of the residents to a newly built center on the grounds of a general hospital in Athens.

Dr KP Kyriakis of the West Attica General Hospital and Leprosy Center in Athens has many diaries of residents which chronicled the horrible conditions of their existence on Spinalonga. According to Dr Kyriakis, the Greek government is currently excavating the island for archeological purposes and plans to restore the Venetian fortress to museum quality. I mailed the above data on Spinalonga, as well as information on Kalaupapa Settlement on Molokai Island and the Gillis W Long HD Center in Carville, Louisiana, to the tour guides.

Our final stop on the tour of the "Land of Myth" was in the great city of Athens. Besides taking the sights of Olympic Stadium, museums and the Acropolis, I visited the only Leprosy Hospital of Greece. I had the privilege of meeting with Drs KP Kyriakis, George Kontochristopolis and Demetrius Panteleos and briefly interviewed Maria Vacenaki, an 80-year old ex-resident of Spinalonga.

The medical staff noted that the incidence of leprosy in Greece has declined to almost negligible percentages during the 20th century even though the country has not initiated any eradication programs. The biggest problem appears to be in persons effectively treated with MDT neglecting to follow instructions for follow up examinations. Additionally, persons living in rural areas do not consistently follow treatment requirements, thus they may be "required" to become inpatients at the center until after repeated negative tests. Their stay at the hospital is designed to emulate their natural home as much as possible, thus many bring their gardening tools and chickens.

Currently, Greece has approximately 1,000 persons who have or are being treated for HD, with 3-5 new cases per year. However, there is still so much fear of the disease, with physicians expressing little interest in this specialty, that those newly diagnosed are "still placed in isolation and the staff drapes their bodies with caps, gloves, gowns, etc." The three physicians added that the Greek Orthodox Church has been very supportive of persons with HD, especially since the stigma has been perpetuated through

various religious sects.

Prior to the residents of Spinalonga being moved to Athens, the government built a spacious building with modern conveniences and readily available medical care. The facility, named "The Center for the Rehabilitation of Leprosy Patients" was in the rear of the spacious acreage designated for the West Attica General Hospital, colored differently from other buildings and encircled with a cyclone fence.

The residents continue to receive a small stipend from the government, but the original "Center..." is now abandoned and residents live in a more modern building approximately 40 yards from their "first home" in Athens. The average age of the residents is 75, all have HD related disabilities and their rooms are filled with religious icons.

Maria Vacenaki resided at Spinalonga from 1943-1957. She was 28 years old when diagnosed after a doctor in her village in Crete noticed that she had lost her eyebrows, a common trait among those with HD. She eventually married a young man she had previously admired from afar..." a young man from a neighboring village also forced to go to Spinalonga."

Ms Vacenaki described life on Spinalonga as "pleasant", even though everyone worked hard to survive, many were sick, families were separated and she lived "a decent life with only my clothes and two wooden chairs as our possessions". She did not feel bitterness about her "imprisonment" and emphasized that "leprosy is not hereditary because many women had children and none of the children became ill (with HD)". She added that her experiences were, "as God wills."

She and her husband declined Greece's invitation in 1957 to move to Athens and instead returned to her village on the island of Crete. She described finding her home in the same condition as when she was "escorted to Spinalonga". The villagers initially had expressed fear and then felt that a miracle had occurred and welcomed her back to the community and her church.

In 1989, Ms Vacenaki had gone to a physician who because of a nodule on her breast and knowing her history, urged her to go to the Leprosy Hospital in Athens. Upon arriving at the facility, the doctors discovered severe ulcers to the bottom of her feet and she chose to remain at the hospital. I told Ms Vacenaki that she reminded me of many beautiful ladies, all old enough to be my mothers, which I have met at other "hospitals" throughout the world and bid my farewell with a hug and a kiss.

Later that evening after visiting Ms Vacenaki, we boarded a plane for our return trip to the US. Thinking that I was through hearing the "I" word, the plane had a

complimentary movie titled "Music From The Heart" with Meryl Streep. In the movie, Ms Streep's character has a conversation with a friend who describes the Bronx in New York City as a "leper colony". My new found friends, sitting in front and to the side of me booed and gave the thumbs down - telling me, with a big smile, that they knew better.

We arrived home on the evening of February 11th. Realizing that on Sunday, February 13th, all churches following the Testament were scheduled to have a reading relating to "lepers", I had written to my Bishop and Pastor months before. I had encouraged them to use this time to educate parishioners about the severe and unjust negative connotations about the "I" word. Well, my pastor chose not to acknowledge my request and instead used the "I" word ten times in his written message to the parishioners and 13 times in his sermon. When I met with him after mass and asked him why he chose not to use this opportunity to educate the church members, he responded by saying, "if I listened to everyone about how I should preach I will never be able to deliver my own sermon" and proceeded to turn his back. I left the church with my family feeling both anger and emotional pain. My efforts, I thought, to dispel myths about HD seem to be more effective away from the community I call "Home."

I was, however, rewarded with compassion and understanding the next day. Many of my friends and colleagues excitedly talked to me about the sermons at their respective churches. The sermons included accurate information about HD. They praised their church leaders for their willingness to educate the community about leprosy and all encouraged me to continue my role as advocate on behalf of other persons affected by leprosy. **We should all be advocates.**



José Ramirez, Jr. and Dr Türkan Saylan

# Stanley Stein -- He lived to Serve Others

Gems from past issues  
Jan - Feb, 1968

Stanley Stein, one of the great fighting editors of all times, has lost his last fight.

The man who spoke for millions of voiceless sufferers from Hansen's Disease throughout the world in their battle to be treated as human beings, died on December 18, 1967, in the USPHS Infirmary at Carville.

For thirty years he boasted he had been living on borrowed time, and his medical friends agreed. In the mid-1930's a malaria epidemic that struck down half the patients at Carville nearly finished him. In 1937, after months of physical agony and mental anguish, iritis made him totally blind--ironically just a few years before the discovery at Carville of the sulfone therapy that today prevents blindness caused by Hansen's bacillus.

Nerve involvement robbed him of the sense of touch over most of his body. To avoid scalding himself he used to test his bath water with his rear end, one of his remaining sensitive areas. Anesthesia of his finger tips deprived him of reading braille.

Injuries to his insensitive hands increased the rate of bone absorption and many of his fingers were shortened.

In 1961 he broke an arm. While his arm was still in a sling, he slipped and broke his hip. The damage was patched up, he wrote, "with stainless-steel pins, and perhaps a few nuts and bolts." The repairs were effective enough so that the following year he was able to fly to New York to work with his collaborator on his autobiographical *ALONE NO LONGER* which Funk & Wagnalls published in 1963.

In 1965 the indomitable editor was suspected of having amyloidosis, a disorder of starch metabolism which was never confirmed. However his strength began to ebb and his health slowly deteriorated over the next two years.

With the "Maccabean courage" he always attributed to his mother, Stanley Stein met all these afflictions with perfect equanimity--until he began to lose his hearing. He then recalled having interviewed Heleen Keller, born blind and deaf, when she came to Carville in 1945.

"If the jinn with the lamp should offer to restore one of your senses," the editor who had been blind less than ten years asked Miss Keller, "which one will you choose?"



"My hearing," she replied, "for I see through the eyes of my friends."

Miss Keller also retained her sense of touch. She could read Braille. She could feel and appreciate the beauty of form.

Stanley Stein's ears were his last link with the world. What would he do without his talking books, his newscast, the stimulating talk of friends? The despair he must have felt did not dampen his spirit. In the last few months when his waning strength sent him to the Infirmary for blood transfusions, his work was slowed but not stopped. Although his limbs were racked by arthritic pain, he realized his hour was growing late, and he drove himself to conclude unfinished business. From his infirmary bed he dictated letters to Africa, to Japan, to India regarding publication of a Mahratti translation of *ALONE NO LONGER*. In consultation with Managing Editor Louis Boudreaux and Editorial Secretary Ernest Dennis he drew up plans for the future of *The STAR* to be forwarded to Dr. Brubaker, director of the hospital.

On the morning of his death, he was still working, going over his mail, dictating answers to Ernest. When he complained of not feeling up to snuff, Ernest suggested taking a break.

"Very well," said the editor. "Be here at ten tomorrow."

Tomorrow never came for Stanley Stein. Shortly after three that afternoon he gave up the fight.

The autopsy indicated the cause of his death as "renal insufficiency"--in other words, kidney failure. There was also evidence of congestive heart failure which he had suffered several times before. According to Dr. Richard E. Mansfield, Carville pathologist, he did not die of leprosy.

Stanley Stein, who had devoted much of his Carville life to encouraging leprosy research, wanted an autopsy so that his death, too, might contribute something to scientific knowledge. For more than thirty years he had been a human guinea pig.

Whenever a new drug was being tested, he had offered himself for experiment. Ironically, none of them did him much good. If they benefitted others as a result of his acting the guinea pig, he was satisfied. It was his mission to serve.--L.G.B.

## Stanley Stein's Legacy To Carville

Stanley Stein's long painful and heroic fight against the relentless personal attrition of Hansen's bacillus was more than matched by his stubborn vigor of his indignant crusade for justice on behalf of his fellow patients at Carville and throughout the world. Sometimes alone, more often through *The STAR*, and frequently with the immense influence of the American Legion, Forty and Eight, other veterans' organizations and their auxiliaries, he achieved revolutionary improvement in the treatment of what he termed "so-called leprosy" sufferers. Let's look at the record of one-third of a century.

- Removal of the barbed wire from the Carville fences.
- Establishment of a branch post office at the hospital.
- Granting to Carville patients the right to have telephones.
- Restoration of the patients' right to vote.
- Repeal of the Louisiana Law which falsely called Hansen's disease a quarantinable contagious disease.
- Abolition of compulsory segregation.
- Repeal of the ban against Carville patients using public transportation.
- Abolition of the Carville jail for "absconders."
- Repeal of the ban against marriages between patients, and the establishment of housekeeping quarters for married couples.
- Granting of week-end passes and month-long vacations from Carville.
- Establishment of the medical discharge.
- Encouragement of visitors and the creation of patient guides
- Establishment of branches at the hospital of such national organizations as the Lions Club, American Legion and the Forty & Eight.
- Persuasion of encyclopedias to correct outdated, erroneous, and unscientific entries under "leprosy" the addition of and cross-reference under "Hansen's disease."
- Continuing campaign against us of the odious word "leper."
- Transformation of *The STAR*, originally started as a local moral builder like the Carville Little Theatre Group (also created by Stanley Stein in his first year of residence) into a world-wide educational influence. ★



# OCULAR LEPROSY\*

Dr Margreet Hogeweg  
Consultant Ophthalmologist-Netherland Leprosy Relief  
Department of Ophthalmology  
Leiden University Medical Centre P.O. Box 9600  
2300 RC Leiden, The Netherlands

This is the first time that ocular leprosy has been included in the series of keynote lectures in an International Leprosy Congress. An overview of the present outstanding issues is presented.

**Blindness in leprosy.** In 1998, Courtright estimated a total number of 350,000-400,000 blind leprosy patients, including PAL's (<sup>1</sup>). This was based on the assumption that 1.5%-2% of the blindness is directly due to leprosy and another 2% due to nonleprosy causes, mainly age-related cataract. Blindness by WHO standards is a visual acuity (VA) of <3/60: "unable to count fingers at a distance of 3 meters," with the better eye. It is not "complete blindness" such as no perception of light. The Indian cut-off point for "blindness" is <6/60: "unable to count fingers at 6 meters," with the better eye. The same VA <6/60 is used as the cut-off point for disability grade 2.

Surveys done before 1980, before the introduction of multidrug therapy (MDT), reported eye complications in as much as 50%-90% of the leprosy patients and blindness in up to 50%. It was in such a leprosarium that I, many years ago, personally got interested in ocular leprosy. In very remote places, such percentages may still exist.

In control programs, after implementation of MDT, potentially sight threatening lesions (PST) are reported in 15%-20%; blindness, in 1%-3%. That is about double the level of blindness in the general population, in poor developing countries, of 0.8%-1%.

Surveys on eye complications and blindness in leprosy are prone to methodological problems: 1) Definition of patients: only active cases or including PAL's.

2) Location of survey: There are large differences in eye complications and blindness, depending on the location of the study: a) in field programs; b) in leprosy hospitals and ulcer wards; c) in leprosy settlements, where disabled, elderly patients with long history of disease cluster. Eye complications will be comparatively low in field programs, but high in leprosy settlements.

3) Inclusion of eye conditions: a) only PST lesions due to leprosy; b) also nonblinding lesions due to leprosy; c) nonleprosy eye lesions. Example: inclusion of madarosis or not? Other nonblinding nonleprosy conditions? This will make large differences.

4) Prevalence (existing lesions), or incidence (new lesions within a certain period in time). One study (<sup>2</sup>) shows that blind leprosy patients have a 4.8-fold excess risk of dying compared to nonblind leprosy patients of the same age. This is one reason why we see comparatively few blind leprosy patients.

**Eye Complications.** Eye complications are caused by the same mechanism that caused complications in general in leprosy: a) type 1 reaction: lagophthalmos and corneal anesthesia; b) type 2 reaction: acute iritis and scleritis; c) infiltration and secondary atrophy: a series of extra- and intra-ocular lesions. The latter two are only seen in multibacillary (MB) patients.

**Potentially sight-threatening lesions in leprosy (PST lesions).** While studying ocular leprosy, it is important to distinguish between potentially blinding versus nonblinding and less important lesions. Therefore, the term potentially sight-threatening lesions (PST lesions) has been coined.

Lesions such as lagophthalmos and exposure keratitis, corneal hypesthesia, acute and chronic anterior uveitis (iridocyclitis), and (secondary) cataract are located in the anterior part of the eye, up to the level of the ciliary body and lens. Eye lesions in leprosy are therefore comparatively easy to diagnose with a normal torchlight, cotton wool and a short-acting dilating eye drop to demonstrate posterior synechiae (adhesions between iris and lens) as a result of anterior uveitis.

**Visual acuity and patient card.** Assessment of visual acuity is the single most important examination in ophthalmology. It should be realized that loss of vision is the same handicap to the patient, whether due to leprosy or to other causes not related to leprosy. Severe visual impairment or blindness may hamper or preclude self-care and is, therefore, more disabling in leprosy patients than in the general population.

Only 56% of the ILEP-supported programs reported to measure VA in a POD survey in 1995 (<sup>3</sup>). One of the problems is that most patient cards actually do not require assessments of visual acuity. For eyes, only facial nerve function and "red eye" are routinely assessed. In order to improve eye care in leprosy, routine assessments of VA, at least at intake and release from treatment (RFT), should be included. In "care after cure patients" older than 50 years, VA should be assessed annually.

The cut-off point for referral and for disability grade 2 is VA

<6/60 (unable to see the upper line on the letter-or E card or unable to count fingers at 6 meters).

**Disability grading in eyes (1987-1997).** In the WHO reporting system only disability grade 2 is of importance. For eyes, up to 1997, only VA <6/60 was considered disability grade 2. Since VA was not routinely assessed, the result was definitely an underestimation of eye complications in leprosy in the official WHO statistics.

Since 1997 the grading system for eyes has been changed and—in line with the general disability grading system—“visible deformities” of the eye, such as lagophthalmos, iritis and corneal opacity, have been included in grade 2, apart from VA <6/60. This should have led to more reporting of disability grade 2, for eyes and hopefully, more attention to eye care, but no data regarding this have been published.

**Cataract.** As a result of increasing life expectancy, eye-related cataract has become the most important cause of blindness worldwide. Age-related cataract is also the most important cause of blindness in leprosy nowadays, in particular among PAL's. For a cataract-blind patient self-care becomes impossible, as he or she cannot avoid, or take care of, injuries and ulcers. In a recent study from Korea (4), cataract was responsible for 87% of the new cases of blindness in an 11-year follow-up study.

Leprosy patients, especially MB patients, have an extra risk of cataract due to the use of systemic steroids for reactions or secondary to iritis. It should be noted that steroids-induced cataract is not a reason to stop steroid treatment for reactions. Cataract can be operated successfully at a later stage, whereas the nerve damage caused by reactions cannot be repaired. A study from Uganda (5) has shown that small pupils, as a result of chronic iritis in MB patients, increase the risk of blindness due to cataract threefold, because even small central lens opacities will greatly influence visual acuity in patients with small pupils.

Poverty and stigma lead to difficulties in access to cataract surgical services. Cataract-blind leprosy patients have therefore less chance of getting surgery than the cataract-blind in general.

**Cataract surgery.** Apart from the time proven ICCE with spectacles and ECCE with spectacles or artificial lens implantation (IOL), new techniques have recently been developed, such as phako-emulsification and small incision sutureless non-phako surgery, both with IOL implantation. A collapsed nose is an extra factor in favor of IOL, surgery because of the lack of support for heavy spectacles. The same applies to severely damaged hands, causing difficulty in handling the spectacles.

Several comparatively small studies have shown that cataract surgery with IOL implantation can give good results in leprosy patients under favorable conditions. In age-related cata-

ract, without intra-ocular complications, there should be no difference in outcome of IOL surgery compared with the general population.

The risk of intra-ocular infection in the case of co-existing lagophthalmos, or in case of ulcers elsewhere, may have increased, but no data are known.

Studies on cataract surgical coverage, barriers to cataract surgery for the patient and outcome of surgery are important to community health interested ophthalmologists and can also be applied to leprosy patients.

**Cataract surgical coverage.** Cataract surgical coverage is a “measure of service.” In this case, it is the cataract surgery actually performed compared to the need for surgery. In other words, operated aphakic or pseudophakic patients (after IOL surgery) in the numerator, divided by the total number of cataract patients, including operated patients, in the denominator.

$$\frac{\text{service}}{\text{need}} = \frac{\text{aphakic and pseudophakic patients}}{\text{cataract blind + aphakic and pseudophakic patients}} \times 100\%$$

For example, if in the study population there are 50 operated patients and no patients with blinding cataract, the cataract surgical coverage is 50/50 = 100%. If, however, there are 20 operated patients and 30 patients with blinding cataract, the cataract surgical coverage is 20/(30 + 20) + 20/50 = 40%: 40% of all cataract patients have been operated. The same type of calculation can be applied to other necessary surgery in leprosy.

To assess surgical coverage, a population-based survey is needed. In case of cataract in people older than 50 years, since this age group is most at risk for cataract blindness, such a survey is feasible in particular in a confined catchment area such as a leprosy settlement or, for example, within one's own control program, including RFT patients.

Under very favorable and exceptional circumstances, with a well-equipped eye department and an ophthalmologist especially assigned to a leprosy program, free surgery and short distances to the hospital, cataract surgical coverage was 80% in a study in Korea (6). It would be highly interesting to repeat this study in other settings. Most probably, the outcome will be different.

**Barriers to cataract surgery.** Distance, poverty and stigma play an important role in the access PAL's have to cataract surgery.

Outreach or “camp” surgery will provide the lowest barriers to patients, since it is near the patient's home and low-cost or free, but the quality of the outcome should be strictly monitored.

Another barrier is surgical capacity. Although in India “blindness” is defined as VA <6/60, and disability grade 2 for leprosy also as VA <6/60, the criteria for free cataract surgery in outreach or eye camps is often only at the level of a bilateral VA of <1/60 (unable to count fingers at one meter). The patient has to be almost completely blind before qualifying for surgery. By that time, the patient has lost any earning capacity he/she may have had. The reason is that the service can otherwise not cope with the large number of patients.

Certainly, leprosy patients with loss of sensation in hands and feet should be operated earlier. Leprosy programs should establish cooperation with the local eye care services for referral of patients. Charity and service organizations, and in India District Blindness Control Societies (DCBS), can be approached for funding, possibly including IOLs.

Other reasons for not having cataract surgery: a) The leprosy staff may be unaware of poor VA in a patient since VA is not routinely measured and patients do not present because they may think that the leprosy services cannot do anything for eye problems, b) Rural people may not feel the need for cataract surgery at the 6/60 level, but only if VA drops to <3/60. c) There may be medical reasons for not having surgery. However, in case of ulcers it should be emphasized to the eye surgeon that a blind leprosy patient is in a vicious circle: exactly because he is blind, he cannot avoid injuries and ulcers. Such patients will always have ulcers. Cataract blindness in leprosy patients should be restored with priority, even in the presence of clean wounds. d) Finally, patients may be afraid of poor outcome, and the surgery may be more difficult in case of small pupils and previous iritis. Leprosy patients should only be operated by eye services with a good reputation, and the postoperative results should be monitored.

**Visual outcome after cataract surgery.** Visual outcome in age-related cataract in leprosy patients should be comparable to the outcome in the general population since they are the great majority of cataract-blind eyes.

Visual outcome in case of complicated cataracts, mainly in MB patients, is not well known, and even less known in the case of IOL surgery in complicated cataract. Several authors have reported more complications during and after surgery, in particular in relation with uveitis and in darker, more pigmented eyes. Small pupils, as may exist in long-standing MB leprosy, will make cataract surgery more difficult because the pupil cannot be properly dilated during surgery.

The outcome of surgery in complicated cases in outreach or camp surgery is not known either. A well-controlled multicenter study is urgently needed on the outcome of IOL, surgery in MB patients compared to IOL, surgery in the general population, in field circumstances, near to where the patients live, and with sufficient follow up (6).

**Lagophthalmos.** Preliminary results from the “LOSOL study” on incidence of eye complications in leprosy under MDT indicate that all new cases of lagophthalmos appear in the first 6-12 months of MDT, with an overall incidence of about 2%. Alternatively, lagophthalmos is already present at the time of first presentation.

From two studies on patches, reactions and facial nerve damage in paucibacillary (PB) as well as in MB patients (8,9) it becomes clear that almost all lagophthalmos is the result of “significant” facial patches around the eye in type 1 reaction and subsequent damage to the underlying facial nerve. Only a maximum 10% of the borderline patients show such patches.

Lagophthalmos is by and large preventable by the timely use of prednisolone for facial patches in reaction. Lagophthalmos of recent onset, usually with still visible reactive facial patches, can often be improved or cured, and vice versa, patients without facial patches are at almost no risk of developing lagophthalmos.

Lagophthalmos is much less common in lepromatous than in borderline leprosy patients and, in the above study (9), was seen almost exclusively in long-standing lepromatous disease. The mechanism of lagophthalmos in lepromatous leprosy is not clear.

For the prevention of lagophthalmos, health workers should concentrate on patients with facial patches. Health education to these patients, careful examination for reaction and early *m.orbicularis* weakness, with timely prescription of corticosteroids, should prevent or considerably reduce facial nerve damage.

In the POD survey of 1995, 91% of all ILEP-supported programs reported to routinely check lid closure. Contrary to VA testing, this is required on the patient card as a part of routine testing of the motor nerve function. However, only 47% offered any lid surgery.

**Treatment of lagophthalmos.** As in nerve damage elsewhere, prednisolone is most effective in facial nerve damage of less than 6 months’ duration.

Cut-off points for conservative treatment versus surgical treatment in lagophthalmos are arbitrary. No long-term prospective studies on the development of exposure keratitis in relation to lid gap have been published. Generally, cut-off point of 5-mm lid gap in mild closure are used as an indication for lid surgery. These values more or less coincide with exposure of the lower part of the cornea. However, values ranging from 4 mm to 10 mm have also been mentioned.

Conservative treatment consists of protection by sunglasses, blinking exercises and “think blink.” It can be supportive by artificial tears. Constraints in conservative treatment include:

a) constant watering, due to malfunctioning of the tear pump and laxity of the lower eyelid, or ectropion; b) foreign body feeling because of dryness of the lower part of the cornea; c) any lagophthalmos is a cosmetic blemish; d) sunglasses may break, get lost or be sold; and e) artificial tears may be too costly in the long run and therefore not feasible. However, the eye itself is usually not at risk in lid gaps in mild closure of <5-6 mm, provided corneal sensation is not impaired.

Which is the best surgical method? Remarkably few studies have been done on the effectiveness of lid surgery. Various methods are in use but mostly on small samples with inadequate follow up and not compared to "no surgery." There is no "golden standard" to compare with. The most commonly performed surgical method in lagophthalmos, up to today, is temporal tarsorrhaphia because it is the simplest.

Different patterns of lagophthalmos with, for example, different grades of laxity of the lower lid, need different types of surgery. Surgery should best be individually geared.

Static lid surgery primarily aims at corneal protection. Tarsorrhaphia can be a cosmetic blemish, in particular in unilateral cases. Extensive tarsorrhaphia causes a troublesome loss of temporal field of vision for the patient. Other techniques include various wedge excisions of the lower eyelid, medial tarsorrhaphia and tarsal strip procedures. Also gold weights in the upper lid are used in order to narrow the lid gap and enhance orbicularis function, but this is usually too costly. Often multiple procedures are necessary. Even so, a considerable residual lagophthalmos may remain.

In dynamic lagophthalmos surgery, a well done temporalis muscle transfer (TMT) can give excellent cosmetic results. Patients can blink, although usually no spontaneous blink habit develops. To be successful, it needs an excellent surgeon, a well-motivated patient and, preferably, good corneal sensitivity. The main disadvantages are the level of surgical skills that is required, often by a plastic and reconstructive surgeon, the intensive physiotherapy needed, rather long admissions and the potential for complications, such as entropion, ectropion or narrowing of the lid gap.

**Lagophthalmos surgical coverage.** For lagophthalmos also for surgical coverage can be assessed: lagophthalmos patients operated with satisfactory result, divided by patients in need of lagophthalmos surgery (or in need of repeat surgery), plus, the successfully operated patients.

In the Korean study<sup>(10)</sup> with the same favorable conditions as for the cataract surgery, the surgical coverage was 57%, if calculated with "any patients ever operated for lagophthalmos" as the numerator. Surgical coverage was only 26%, if taken into account that 53% of the operated patients still had a residual lid gap of >5 mm and, therefore, in fact still needed additional surgery.

**Outcome of lagophthalmos surgery.** As mentioned, 53% of the operated patients in the Korean study still had a >5-mm lid gap after lagophthalmos surgery through various methods, showing how rather unsatisfactory the result of lid surgery often is; 28% were not satisfied with the result themselves and 20% would not recommend lagophthalmos surgery to others.

It would be interesting to design such outcome studies, based on residual lid gap, elsewhere. Problems in cross-sectional population-based studies of outcome of lagophthalmos surgery include: a) no data on the surgical method available; b) no data on presence of exposure keratitis at the time of initial surgery; and c) no data on visual acuity at the time of initial surgery. To answer these problems, long-term prospective studies on well-documented patients, including surgical technique, are needed and highly recommended.

The barriers to lagophthalmos surgery in the Korean study were: no knowledge about the possibility of surgery, costs, distance, service perceived as poor quality, and no need for surgery felt.

Recommendations for lagophthalmos surgery are: a) semi-standardized criteria for selection of patients for lid surgery for health workers are needed, such as mm lid gap in mild closure or presence of exposure keratitis; b) success of surgery to be monitored on residual lid gap; and c) each leprosy program should offer lagophthalmos surgery as part of the POD program, either themselves or through the ophthalmic services.

**ENL, clofazimine and uveitis.** It is a definite clinical impression that acute iritis and acute scleritis are less common since the introduction of MDT. This is attributed to the routine use of clofazimine which has led to a reduction in the frequency of erythema nodosum leprosum (ENL) reactions as well. Binding bilateral scleritis, with secondary glaucoma, in recurrent severe ENL used to be among the most important causes of blindness in leprosy. Nowadays this has become a rare complication.

Uveal disease, with keritic precipitates, cells and flare, and pupil shape abnormalities, continues in MB patients, in spite of MDT. According to preliminary LOSOL findings, cumulative incidence of any uveitis is about 5% at the end of MDT and increases to about 13% 2 years after RFT.

**Corneal hypesthesia or anesthesia.** Corneal hypesthesia is difficult to quantify unless measured by the Cochet-Bonnet monofilament esthesiometer. It may be overdiagnosed at times or confused with incomplete blinking, as in the case of lagophthalmos. It can sometimes be seen in lepromatous patients with a long history of disease. In that case it is probably the result of infiltration and secondary atrophy of the corneal and ciliary nerves and comparable to glove and stocking anesthesia. In these cases there can be severe bilateral corneal hypesthesia without lagophthalmos.

In combination with lagophthalmos, one can imagine two

mechanisms: direct damage to the trigeminal nerve at the time of facial nerve damage, or indirect damage as a result of long-standing exposure. No studies have been published on corneal hypesthesia occurring in a case with a reactive facial patch or in recent lagophthalmos. It is not known if corneal hypesthesia may recover by systemic steroids.

**Progression of eye disease.** The final results of the LOSOL, study on incidence of eye complications and long-term outcome in MDT are still to be published.

In another study (2), progression of eye disease over a period of 11 years in RFT patients initially free of eye involvement happened in 14.7%, either as keratitis, synechiae or lagophthalmos. In addition, from those initially free of cataract, 5.7% developed bilateral blinding cataract. Of the incidence cases of new blindness, 87% was due to cataract. It is thus important that “care after cure” disabled leprosy patients receive routine eye examinations, including visual acuity, at least once a year.

**Research priorities.** Research priorities should include: a) Cataract: studies on surgical coverage, outcome with /without IOL, and barriers to cataract surgery for leprosy patients in different settings are highly recommended. Lagophthalmos: studies are needed on indications and cut-off points for surgery, best technique, and long-term outcome, in combination with lagophthalmos surgical coverage, and barriers to lid surgery. c) Operational research:: studies on best implementation of eye care in POD activities and integration of eye care for leprosy patients into the general eye care services.

### Recommendations.

- The leprosy services should be the “watch dogs” for any sight-threatening eye disease.
- Facial patches in reaction and recent lagophthalmos should be treated with a course of prednisolone.
- Each leprosy program should have a collaborative agreement with a nearby eye care service for referral of patients who need specialist help, in particular for surgery.
- A policy giving priority to leprosy patients for cataract surgery should be developed in collaboration with the local eye care services.
- Eye care services and leprosy services in collaboration should provide training in eye care in leprosy to leprosy staff as well as to eye care staff and, together, should provide guidelines for treatment.

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### Network of Support



#### for Individuals Affected by Hansen’s Disease.

Together with **IDEA**, the International Association for Integration, Dignity and Economic Advancement, I am establishing a network of support for individuals and their families in the United States who are facing the physical and social challenges often associated with Hansen’s Disease. I was diagnosed with Hansen’s Disease in 1997 and, consequently, feel that I can empathize and provide support to others because of the experiences and challenges that I’ve had to overcome and am still overcoming. I can certainly identify with those of you who have had difficulty finding answers to some of your questions, or even asking them at all, as I too have struggled with this. Similarly I know that there are many of you who have had experiences that will help others and sharing these will strengthen our ability to provide support to all who need it. I will personally respond to all emails and telephone calls and will network with **IDEA** and others to provide you with information on available resources and give you referrals if I cannot help. You can access my website at [www.hansensdisease.org](http://www.hansensdisease.org) and email me there or at [admin@hansensdisease.org](mailto:admin@hansensdisease.org) with any questions or concerns that you may have. I also have a toll-free number: 1-866-637-1525. I will be happy to mail out brochures to anyone interested in this network of support. Ultimately, I hope that we can work together to encourage ourselves and others to develop the courage and self-confidence that are essential to successful treatment and leading a normal life in the community.



**Nicole H. Holmes**



Support Group Coordinator, IDEA

# ANTIOXIDANT EFFECT OF VITAMIN E IN PATIENTS ON ANTILEPROSY CHEMOTHERAPY

Vijayaraghavan R, SuriBabu C S, Sekar B, Krishnamurthy K V,  
Narashimmamurthy P, Panda P K, Oomen P K, Vinod Kumar C H D, Jeyarama E,  
Panneerselvam C.\*

## Abstract

Leprosy continues to afflict a large number of people globally. The causative germ *Mycobacterium leprae* affects vital cellular molecules leading to tissue disruption that may cause deformity and disfigurement when left untreated. One of the major mechanisms by which tissue disruption occurs during leprosy is the deleterious effect of free radicals. Nutrition would have a key role in preventing the development of the disease. In the present study, we have investigated the antioxidant status in leprosy patients who are undergoing multiple drug therapy and those who were coadministered vitamin E, an essential nutrient. A significant improvement of the antioxidant status in all the spectrum of leprosy was noticed. Coadministration of vitamin E with multiple drug therapy reduced the level of plasma lipid peroxidation (LPO) which is an index of in vivo free radical production, and activates the antioxidant system. Hence we conclude that exogenous supplementation of the antioxidant vitamin E certainly favors the leprosy patients in protection against the oxidative stress and free radical-driven damage during the chronic course of the disease and antileprosy chemotherapy.

## Introduction

Our body is made up of millions of cells which in turn contain millions of molecules having pairs of electrons. This pairing of the electrons is important in helping to keep the body in a healthy state. This orderly state of affairs can be upset if the body is exposed to too many free radicals. Chemical species having unpaired electrons are considered free radicals, capable of altering biomolecules. The most important in vivo source of free radicals is molecular oxygen itself. The univalent reduction of oxygen biradical results in the formation of many oxygen-derived free radicals like superoxide radical, hydroxyl radical, hydrogen peroxide and alkyloxy radicals. These radicals are short-lived, but highly reactive with the biomolecules. Substances having a spare electron to donate and eliminate the deleterious effect of free radicals are designated as antioxidants (1).

Imbalance between the production of free radicals and the in vivo availability of antioxidants (which scavenge the free radicals that cause damage to cells and biomolecules) might underlie the etiology and complications of leprosy. Antioxidants are small molecules mostly derived from the diet; dietary vitamins present both extra- and intra-cellularly in molar and millimolar range are involved in the maintenance of fundamental metabolic status and homeostasis of the cellular milieu (2). Antioxidants are best supplied by a well-balanced diet. However, many leprosy-affected persons may not always get antioxidant-rich foods like fruits and fresh leafy vegetables everyday, and hence exogenous supplementation of antioxidants has become a necessity (3). Nature also coevolved in providing enzymatic and nonenzymatic antioxidant defense systems like the enzymes superoxide dismutase (SOD), glutathione peroxidase (GPX), glutathione-s-transferase (GST), catalase, glutathione reductase, as well as the nonenzymes vitamin A, vitamin C, and vitamin E. But when there is a deficiency in the antioxidant system, there won't be any protection in the body against the free radical-driven damage to cells and biomolecules (4). Disease prevention by way of specific nutrition is an attractive approach. Nutritional rehabilitation by supplementing with immuno-enhancing, lipid soluble antioxidants (5), guarding against the free radical-driven insult, provides compelling evidence of the efficacy of vitamin E in enhancing antioxidant status. Nonenzymatic antioxidants augment the levels of enzymatic antioxidants, protecting against the free radical-driven insult during the chronic course of the disease and antileprosy chemotherapy.

## Materials and Methods

Oxidant assault has been reported in tobacco smokers, persons with hypertension, diabetes and other systemic ailments. Hence persons with these habits and systemic ailments were excluded from this study. Healthy volunteers of both sexes of different age groups were recruited; they did not have contact with leprosy patients or cardinal signs and symptoms of the disease. Leprosy cases: paucibacillary (PB) (Mild) and multibacillary (MB) (Severe) patients were recruited from the wards/OPD/field areas of Leprosy institute/Leprosy control units, on the basis of their bacillary load as determined by microscopic examinations of their skin smears taken from the lesion-occupied areas, and classified using the Ridley logarithmic bacteriological scale. The study subjects were grouped as follows:

### GROUPS

- Group: I : Healthy volunteers (n=40)
- Group: II : Untreated PB leprosy \*(n=35)
- Group: III : Untreated MB leprosy \*\*(n=26)
- Group: IV : PB Leprosy Cases Kept in PB-MDT (n=19)
- Group: V : MB Leprosy Cases Kept in MB-MDT (n=16)
- Group VI : PB Leprosy Cases Kept in PB-MDT+Antioxidants (n=15)
- Group VII : MB Leprosy Cases Kept in MB-MDT+Antioxidants (n=18)

\*PB = Paucibacillary cases who harbor a limited detectable number of acid fast bacilli (*M. leprae* is an acid fast bacillus). PB constitutes the MILD LEPROSY GROUP. I (Indeterminate leprosy), TT (Tuberculoid type of leprosy), and BT (Borderline Tuberculoid leprosy) cases fall under PB leprosy. \*\*MB= Multibacillary cases (who harbor an innumerable number of *M. leprae*. MB constitutes the SEVERE TYPE OF LEPROSY. BB (Midborderline), BL (Borderline Lepromatous), and LL (Lepromatous Leprosy) cases fall under MB leprosy) (6).

Five ml of venous blood collected by venipuncture from each of the above-mentioned groups in sterile anticoagulated test tubes was processed for the separation of plasma and the hemolysate. The plasma portion was used for biochemical assays of proteins (7), plasma lipid peroxides (8), and the vitamin E status (9). Whole blood was used for the determination of hemoglobin concentration (10). Packed cells remaining after removal of plasma were washed with isotonic saline, and Tris-HCl buffer, pH 7.4 was used to remove the buffy coat. Haemolysis was performed; the erythrocyte ghosts were sedimented by centrifuging at 150,000 rpm for 40 minutes; the supernatant haemolysate was removed carefully and used for the assay of enzymatic antioxidants.

Superoxide dismutase SOD (EC:1.15.1.1), (11), glutathione peroxidase GPX (EC:1.11.1.9), (12), catalase (EC: 1.11.1.6), (13), glutathione reductase (EC: 1.6.4.2), (14) and glutathione-s-transferase GST (EC:2.5.1.18), (15) were assayed as described in the references quoted.

Vitamin E was obtained as a free gift from Soft Caps India Ltd, Chennai (Madras), India, and coadministered with the usual WHO multiple drug therapy (16). RDA (recommended daily allowance) of vitamin E was followed throughout the study; 400 International Units of vitamin E were given orally to leprosy patients undergoing PB and MB MDT. Blood collection was done on day of onset of the treatment, during and after MDT. The enzymatic and nonenzymatic antioxidant levels were estimated using standard biochemical procedures, as mentioned above, and the results obtained were tabulated.

**Table 1**  
**Comparison of mean ± standard deviation among seven groups**

Variables	Group I N=40	Group II N=35	Group III N=26	Group IV N=19	Group V N=16	Group VI N=15	Group VII N=18
<b>LPO</b> Nmol/MDA/L	69.0 ± 3.31	83.8 ± 4.02	91.6 ± 3.59	81.5 ± 1.43	86.6 ± 3.07	74.3 ± 2.60	77.5 ± 2.88
<b>SOD</b> Units/gram/Hb	3744.7 ± 2986.63	2762.6 ± 268.13	1891.5 ± 223.50	2902.7 ± 108.62	2295.0 ± 338.35	3353.5 ± 202.01	3611.5 ± 340.92
<b>GPX</b> Units/gram/GSH Utilised/min	5920.3 ± 278.69	4969.8 ± 264.90	4049.6 ± 124.70	5093.6 ± 145.63	4195.2 ± 175.94	5766.9 ± 107.72	5522.5 ± 296.2
<b>Catalase</b> µ moles of H2O2 Consumed/min	1150.6 ± 195.95	850.6 ± 98.41	639.6 ± 101.25	894.6 ± 43.46	721.5 ± 89.67	1166.4 ± 78.78	1142.0 ± 103.50
<b>G-s-Transferase</b> Units/grams/Hb	2.4196 ± 0.30	1.9868 ± 0.12	1.7184 ± 0.10	2.1960 ± 0.80	1.8775 ± 0.13	2.6056 ± 0.15	2.6630 ± 0.28
<b>GSH</b> Mmoles/L	1.3420 ± 0.23	0.8508 ± 0.13	0.6176 ± 0.09	0.9805 ± 0.10	0.8275 ± 0.80	1.5338 ± 0.07	1.1825 ± 0.06
<b>Vitamin E</b> µ Moles/L	19.03 ± 1.42	15.43 ± 0.74	13.93 ± 0.34	14.97 ± 0.39	14.41 ± 0.33	16.95 ± 4.38	17.63 ± 0.70

### Statistical Analysis

Data are expressed as mean, standard deviation; the data were analysed by one-way analysis of variance (ANOVA) using computerized statistical package SPSS. Each experimental group was compared with respective control groups. When ANOVA indicated significant differences, data were further analysed by Duncan's Test for multiple comparison. Differences were considered significant at  $p < 0.01$ , indicated by using symbols \*.

**Table 2**

**Differences in the sex among the Groups**

SEX	I	II	III	IV	V	VI	VII	TOTAL
<b>MALE</b>	14	18	20	13	17	10	16	108
<b>FEMALE</b>	11	7	5	7	3	6	4	43
<b>TOTAL</b>	25	25	25	20	20	16	20	151

**Table 3**

**AGE (MEAN), S.D**

GROUP	MEAN	S.D
<b>GROU I</b>	33.8	18.90
<b>GROP II</b>	40.1	15.8
<b>GRUP III</b>	31.6	11.8
<b>GROUP IV</b>	41.4	16.7
<b>GROUP V</b>	35.5	7.3
<b>GROUP VI</b>	41.4	16.5
<b>GROUP VII</b>	36.2	8.4



**Table 4**

**Comparison of mean values of LPO**

Source	D.F	Sum of significance	Mean Squares	F value	P value
Between Groups	6	8192.6582	1365.4430	122.9481	<0.00001
Within Groups	144	1599.2420	11.1058		
Total	150	9791.9001			

**Duncan' Multiple Range Test:**

Mean	Group	I	VI	VII	IV	II	V	III
69.037	I	-	-	-	-	-	-	-
74.30	VI	**	-	-	-	-	-	-
77.50	VII	**	**	-	-	-	-	-
81.53	IV	**	**	**	-	-	-	-
83.76	II	**	**	**	**	-	-	-
86.60	V	**	**	**	**	***	-	-
91.64	III	**	**	**	**	**	***	-

**Table 5**

**Comparison of mean values of SOD**

Source	D.F	Sum of squares	Mean Squares	F-value	p-value
Between Groups	6	64447656.9	10741276.1	127.739	<0.00001
Within Groups	144	12108655.5	84087.88		
Total	150	76556312.4			

**Duncan' Multiple Range Test:**

Mean	Group	III	V	II	IV	VI	VII	I
1891.5	III	-	-	-	-	-	-	-
2295.0	V	**	-	-	-	-	-	-
2762.6	II	**	**	-	-	-	-	-
2902.7	IV	**	**	-	-	-	-	-
3353.5	VI	**	**	**	**	-	-	-
3611.5	VII	**	**	**	**	***	-	-
3744.7	I	**	**	**	**	**	-	-

**Table 6**

**Comparison of mean values of GPX**

Source	D.F	Sum of squares	Mean Squares	F-value	p-value
Between Groups	6	71455612.3	11909268	242.602	<0.00001
Within Groups	144	7068929.2	49089.8		
Total	150	78524541.5			

**Duncan' Multiple Range Test:**

Mean	Group	III	V	II	IV	VII	VI	I
4095.2	III	-	-	-	-	-	-	-
4195.2	V	**	-	-	-	-	-	-
4969.8	II	**	**	-	-	-	-	-
5093.6	IV	**	**	-	-	-	-	-
5522.5	VII	**	**	**	**	-	-	-
5766.9	VI	**	**	**	**	**	-	-
5920.3	I	**	**	**	**	**	**	-

Contd next issue

# FROM DAVE'S DESK

## "CARVILLE STAR"

In my last article I advised there were more changes taking place at Carville. The changes have been made, and I want to inform you of the current status of the "The Star."

La Societe got involved with The Star about 61 years ago. It was set up as a patient-only enterprise, to "Radiate the Light of Truth about Hansen's Disease," as Stanley Stein envisioned it. With our support it has continued to do exactly that, and will continue to do so in the future.

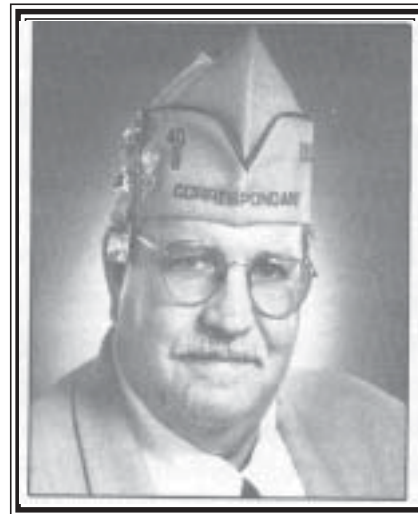
We all know about changes at The Star during the past couple of years, so I will not discuss those at this point. You should know there are no longer any patients to do the work it takes to publish The Star. For the past year or so we have contracted outside help to get The Star out. That was not the idea that Stanley Stein envisioned. He did however envision The Star being around for a long time, and the changes that have been made will help us achieve that goal.

The Star office has moved to smaller office space, and will now move into the electronic age. It will be on line @fortyeight.org. Anyone who has a subscription will receive a letter giving you all the information about how to get it off line. It will still be printed by Franklin Press in Baton Rouge, LA., and will be distributed the same as the Forty and Eighter.

This also means that Emanuel Faria, the Editor, and Bill Kikuchi, the Business Manager, will still do their jobs, but they will not have to print the magazine. Voiture Nationale will maintain the subscription list in Indianapolis, IN. For those of you that have not been receiving your Star, I have found the problem and we are correcting it at Voiture Nationale.

Cost cutting was one of the big benefits that comes from cutting down on the office space at The Star. The equipment will have to be disposed of as it is all out of date. We tried to donate it to the boy's school at Carville, but training them on that old equipment is not acceptable by the state of Louisiana. The present "Equipment and Maintenance" account will be changed to just the "Maintenance Account."

Basically The Star continues to be the voice of Carville, and still needs your support, So I ask that you continue your subscriptions, keep buying the Countries, and keep sending donations to the "Maintenance Fund."



David Rabius

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### Unique Properties . . . (Contd from page 1)

$\beta$ -Lactamase is a constitutive enzyme in mycobacteria, including *M. tuberculosis*. But in *M. leprae* unexposed to  $\beta$ -lactamase antibiotics, no  $\beta$ -lactamase was detected. But the enzyme was detected in bacteria recovered from experimentally infected armadillos treated with penicillin G benzathine to control secondary infections. The enzyme activity persisted when the bacteria were used as inocula to infect other armadillos that received no penicillin. The induced enzyme persists even after the inducing agent is withdrawn; the phenomenon is referred to as de-repression. Short term exposure of the HD organism to  $\beta$ -lactam antibiotics in vitro did not induce the enzyme.

A potent  $\beta$ -lactam/ $\beta$ -lactamase inhibitor complex, ampicillin-sulbatam, [UNASYN - injectable or SULTAMICILLIN - oral (Pfizer)] killed mycobacteria, including drug-resistant *M. leprae* and *M. tuberculosis*. The drug was **bactericidal** to *M. leprae* multiplying in mouse foot pads, *M. tuberculosis* growing in vitro, and in murine experimental tuberculosis. AUGMENTIN (amoxicillin-clavulanate) showed activity only at three times the concentration of UNASYN. Since the concentration of  $\beta$ -lactamase in mycobacteria is far lower than that in Gram-negative organisms, comparatively much lower concentrations of the drug would kill the TB and HD bacilli. Ampicillin/sulbactam could serve as an effective alternative treatment in leprosy and tuberculosis cases, especially those resistant to other drugs. ★

## SOURCES OF HD TREATMENT IN THE UNITED STATES

THE NATIONAL HANSEN'S DISEASE PROGRAMS (NHDP) provides HD care to persons in the United States at 1770 Physicians Park Drive, Baton Rouge, LA 70816 and through the Ambulatory Care Program, which includes the following Outpatient HD Clinics:

### NATIONAL AMBULATORY HANSEN'S DISEASE PROGRAM

AREA	FACILITY	ADDRESS	PHYS/NURSE	APPOINTMENT
<b>BOSTON</b>	Lahey Medical Center	41 Mall Rd. Burlington, MA 01805	Samuel Moschella, MD Stephanie Burns, RN	781-744-5670
<u><b>CALIFORNIA</b></u> LOS ANGELES	LAC, USC Medical Center Attn: Section of Dermatology Room 8440	1200 North State St. Los Angeles, CA 90033	Thomas Rea, MD Helen Mora, RN Robert Jersey, OT	323-226-5240
MARTINEZ	Contra Costa Regional Medical Center Outpatient Clinic	2500 Alhambra Drive Martinez, CA 94553	Sutherland/Saffier, MDs Carol James, RN	925-370-5270 1-800-495-8885 (In state only)
SAN DIEGO	North Central Public Health Center	2440 Grand Avenue San Diego, CA 92109	D. A. Lopez, MD Carmen Rodriguez, RN	858-490-4400
<b>CHICAGO</b>	University of Illinois College of Medicine	Department of Dermatology, (MC 624) 808 S. Wood Street, RM 376 CME Chicago, IL 60612	Carlotta Hill, MD Norma Chelseth, RN	312-996-0734
<b>MIAMI</b>	Jackson Memorial Hospital	Ambulatory Care Center 1611 N.W. 12 <sup>th</sup> Avenue Miami, FL 33136	Anne Burdick, MD Gloria Ingle, RN	305-585-2600
<b>NEW YORK</b>	Bellevue Hospital Center Department of Dermatology Room 17-N-7	462 First Avenue New York, NY 10016	William Levis, MD Aloys Cabrera, RN Louis Iannuzzi, PT, C.Ped	212-562-6096
<b>PHOENIX</b>	Maricopa County Health Dept.	1825 East Roosevelt Street Phoenix, AZ 85006	Ronald Pust, MD Bill Cooper, RN	602-372-6661
<b>PUERTO RICO</b>	University of Puerto Rico Medical School	Department of Dermatology P. O. Box 365067 San Juan, PR 00936-5067	Pablo Almodovar, MD Sonia Santos-Exposito, RN	787-765-7950
<b>SEATTLE</b>	Harborview Medical Center	2 West Clinic - 359930 325 9 <sup>th</sup> Avenue Seattle, WA 98104	James P. Harnisch, MD Rebecca Finch, RN Tom McClure, PT, CH	206-731-5100
<u><b>TEXAS</b></u> DALLAS	Dallas County Health Department	2377 N. Stemmons Freeway, Ste. 522 Dallas, TX 75207-2710	Jack Cohen, DO Nancy Bernstein, RN	214-819-2010
<b>HOUSTON</b>	Houston Health & Human Services Dept.	1809 North Main Houston, TX 77009	Terry Williams, MD Eileen Walton, RN	713-504-0256
SAN ANTONIO	Texas Center for Infectious Disease	2303 S. E. Military Drive San Antonio, TX 78223	Robert N. Longfield, MD Debbie Mata, RN	210-534-8857
HARLINGEN	South Texas Health Care Center OPCL	1301 Rangerville Road Harlingen, TX 78550	Richard Wing, MD San Juana Thompson, RN	956-423-3420 ext. 351

**Other Sources:** State of Hawaii Department of Health  
3650 Maunalei Ave., Suite 205  
Honolulu, HI 96816  
Phone: 808-733-9831

Mike Maruyama, MPH, Branch Chief  
Barbara Yoshioka, R.N.  
Program Manager  
Fax: 808-733-9836

**FOR MORE INFORMATION:** Call the NHDP at **1-800-642-2477** or fax: (225) 756-3760  
Email: [MTemplet@hrs.gov](mailto:MTemplet@hrs.gov)

## FACTS ABOUT HANSEN'S DISEASE

BULK RATE  
US POSTAGE  
PAID  
PERMIT #1  
CARVILLE, LA,  
70721

### What is (HD)?

Hansen's disease, erroneously associated with biblical leprosy, is a complex infectious disease which, although recognized for more than two thousand years and found to be caused by a bacterium over a century ago, is not completely understood. Dr Gerhard Armauer Hansen, Norwegian scientist, first discovered the HD bacillus in 1873. Considerable progress has been made during the last 40 years, so that today we can treat the majority of cases without undue difficulty and counteract most of the fears generated by the folklore surrounding this disease.

HD is essentially a disease of the peripheral nerves, but it also affects the skin and sometimes other tissues, notably the eye, the mucosa of the upper respiratory tract, muscles, bones and testes.

There are both localized and disseminated forms of HD. If left untreated, HD causes nerve damage, which can result in loss of muscle control and crippling of hands and feet. Eye involvement can result in blindness.

### Where is HD Found

In 1994 the World Health Organization estimated that there were 2.4 million cases of HD worldwide with 1.7 million cases registered on treatment. The estimates for 1985 were 10 - 12 million and 5.4 million respectively. According to these estimates, in 1994, 70% of those who should be on treatment are now being treated. In 1992 there were 690,000 new cases reported and in 1993, 591,000 cases. There are also an estimated 2 - 3 million cases who have completed treatment but who still have residual disabilities who are not included in the above 1994 totals. The largest numbers of Hansen's disease patients continue to be in Southeast Asia and Central Africa with smaller numbers in South and Central America. The largest number of patients in the Western Hemisphere are in Brazil.

In the United States there are approximately 6,500 cases on the registry which includes all cases reported since the registry began and still living. The number of cases with active disease and requiring drug treatment is approximately 600. There are 200 - 250 new cases reported to

the registry annually with about 175 of these being new cases diagnosed for the first time. The largest number of cases in the US are in California, Texas, Hawaii, Louisiana, Florida, New York, and Puerto Rico. There are still approximately 150 cases at the Gillis W Long Hansen's Disease Center at Carville, LA, the only institution in the US exclusively devoted to Hansen's disease. The center functions as a referral and consulting center with related research and training activities. Most patients in the US are treated under US Public Health Service grants at clinics in major cities or by private physicians. (See inside back page for listing of clinics.)

### How Does HD Spread?

While this aspect of the disease remains a medical mystery, the most commonly accepted theory is that it is transmitted by way of the respiratory tract, and abraded skin. The degree of susceptibility of the person, the extent of exposure, and environmental conditions are among factors probably of great importance in transmission. Most specialists agree that 90% or more of the world's population have a natural immunity to the disease. Persons working with HD contract the disease only rarely. Cases of HD which respond satisfactorily to treatment become noninfectious within a short time.

### How is HD Treated?

Although the sulfone drugs, introduced at Carville in 1941, continue to be an important weapon against the Hansen bacillus the rising incidence of sulfone resistant disease necessitates treating all patients with more than one drug. Usually rifampin and sometimes clofazimine or ethionamide are given in addition to dapsone. Treatment rapidly renders the disease noncommunicable by killing nearly all the bacilli and these dead bacilli are then cleared from the body within a variable number of years.



Gillis W Long  
Hansen's Disease Center

Guided Tours Daily  
10:00 AM and 1:00 PM

## GET TO KNOW THE FORTY & EIGHT



The Forty & Eight, an honor society of legionnaires created in 1920 and *The Star's* primary funding organization, draws its origin from World War I. Millions of American soldiers in France were transported to the front in narrow French box-cars, called "Voitures," which would only hold 40 men or 8 horses. Remembering the close brotherhood of those box-car days, La Societe des Quarante Hommes et Huit Chevaux

(The Society of 40 men and 8 Horses) was formed and local Voitures began organizing as outstanding Legionnaires were invited into membership. Membership is still by invitation only.

Dedicated to the needs of their fellowman, the Forty & Eight raises funds and support not only *The Star*, but funds a national nursing scholarship program, various child welfare programs, provides aid to veterans and continues to promote Americanism at both local and national levels.