BIBLICAL CURSE, MODERN MUTILATION:

THE PLASTIC SURGEON’S ROLE IN LEPROSY in 2005

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The most terrible poverty is loneliness and the feeling of being unloved. Make us worthy, Lord, to serve those people throughout the world who live and die in poverty and hunger. Give them through our hands, this day, their daily bread, and by our understanding love, give them peace and joy. I heard the call to give up all and go into the slums to serve the Lord, amongst the poorest of the poor. It was an order.
Mother Teresa

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And the Lord spake unto Moses and Aaron, saying
When a man shall have in the skin of his flesh a rising, a scab, or bright spot, and it be in the skin of his flesh like the plague of leprosy: then he shall be brought unto Aaron...and the priest shall look on him, and pronounce him unclean.....When raw flesh appeareth in him, and in the place of the boil there be a spot, white, and somewhat reddish, and it be shewed to the priest;... the priest shall pronounce it unclean; it is a plague of leprosy broken out of the boil... And the leper... his clothes shall be rent, and his head bare, and he shall put a covering upon his upper lip, and shall cry, Unclean, unclean. All the days wherein the plague shall be in him he shall be defiled he shall dwell alone; without the camp shall his habitation be.

Leviticus 13:1-3, 14, 19,20,29,30,45,46
ABSTRACT: PROLOGUE/EPilogue

It is likely that most of you reading this learned about Leprosy from the Bible. Indeed, you may not have learned much else about it except that it is a contagious, mutilating disease. Most doctors have never met a Leper.

In the essay that follows you will learn that:

1. A Norwegian doctor identified the cause of Leprosy, a bacteria, not a curse, in 1873.

2. Mycobacterium leprae is mildly contagious; it does not pass through epidermis.

3. A Scottish dermatologist first used a sulfa Rx in Chingleput, India, for Leprosy: 1943.

4. A British orthopod: identified the deformity as related to nerves; Vellore, India, 1948, introduced tendon transfers for the hand deformity in 1952, and refuted the “dissolving flesh” theory of Leprosy:


6. Though M. leprae is destroyed by antibiotics, peripheral nerve destruction continues.

7. M. leprae has an adhesion molecule that attaches to the G domain of laminin, permitting ingestion of the bacteria by the Schwann cell: learned in 1997.

8. Despite MDT, there are 500,000 new cases of Leprosy in the world per year, 12% of which are in children, and 200 of which are in the U.S.A.: There are 12 millions Lepers in the World and 6,000 in the U.S.A.

Plastic Surgeons can help with reconstruction of the nose, facial palsy, ulceration, tendon transfers, use of innervated flaps, and new peripheral nerve surgery approaches that can prevent or minimize deformity, and restore function.
INTRODUCTION

The dermatologic "definition" of leprosy was given to Moses, and Aaron, his high priest, by God, as described in Leviticus, Chapter 13.¹ It was, by definition, a plague, and the priests first placed the suspected person under quarantine for 7 days, and then banished the person as an outcast to live in what became leper colonies, from which it may be inferred that leprosy was considered infectious.

And the Lord spake unto Moses saying

Command the children of Israel that they put out of the camp every leper, and every one that hath an issue,...Both male and female shall ye put out, without the camp, that they defile not their camps, in the midst whereof I dwell...And the children of Israel did so, and put them out without the camp²

It was recognized that leprosy could run its course, the leper could be "healed", and then the priests could cleanse the leper using "two birds alive and clean, and cedar wood, and scarlet yarn, and hyssop" in a proscribed manner.³

Figure 1. Hyssop, an ancient herb, that had detergent properties.⁴⁵

Hyssop (Hebrew: שׁוֹפֶל̱ שׁוֹפֶל̱ Esov), (Greek: σῶτρος hyssopos), see Appendix 1.
God clearly had the power to cure a person of leprosy, as he did for Naaman. Naaman was in charge of the armies of Syria, and he was a leper. Among his conquests was the village of Samaria, in which lived the prophet Elisha. Elisha instructed Naaman to bathe seven times in the river Jordan in order to be cured. Naaman did so, and was cured (Appendix 2).

God also clearly had the power to give a person leprosy, and he did so as a punishment to the servant of Elisha, who took money as a reward from Naaman. The skin pigment loss of leprosy, in these Mediterranean peoples, is used visually, in the bible, as proof that the God had caused leprosy, e.g. “and he [the servant of Elisha] went out from his [Elisha’s] presence a leper, as white as snow.” God also punished Miriam, after she and Aaron, the high priest, were so arrogant as to think they could interpret the will of God, which they did when Moses, through whom God spoke at that time, was away. After the punishment “Miriam became leprous, white as snow.” With regard to the loss of tissues that was observed in the lepers, Aaron makes reference when he says “Let her not be as one dead, of whom the flesh is half consumed.” And God let her punishment last only 7 days, during which she was outcast from the community. (Appendix 3.)

The third time that God uses leprosy as a punishment, as recorded in the Bible, is related to the life of Uzziah. Uzziah succeeded to his father Azziah’s throne, as King of Israel. Uzziah was just 16. He went on to enlarge the kingdom and build its army, and the wealth of its citizens. And yet, at a time when he was at his peak power, his arrogance led him to attempt to burn incense in the holiest sanctuary of the Temple. At that time, 80 priests attempted to thwart his efforts, and
Uzziah was wroth, and had a censer in his hand to burn incense; and while he was wroth with the priests, the leprosy even rose up in his forehead before the priests in the house of the Lord, from beside the incense altar. And Aziairah the chief priest and all the priests, looked upon him, and behold he was leprous in his forehead, and they thrust him out from thence; yea, himself hasten also to go out, because the Lord had smitten him. And Uzziah the king was a leper unto the day of his death, and dwelt in several houses, being a leper; for he was cut off from the house of the Lord; and Jotham his son was over the King's house, judging the people of the land.  

An example of someone with the forehead lesion of leprosy is given in Figure 2.

Figure 2. Lepromatous form of leprosy has elevated skin lesions on the face.

In the New Testament, the healing of lepers also is reported. In Matthew, the first leper was healed after "Jesus put forth his hand, and touched him, saying be thou clean. And immediately his leprosy was cleansed." The second leper was healed without Jesus having seen the leper.  

Luke reported that Jesus responded to the request of a group of 10 lepers for healing, but only the one, a Samaritan, who returned and "glorified God" was healed permanently.
Leprosy is an ancient disease; known in Egypt, Palestine, India, and Rome. There are records from 880 B.C. warning against marrying the child of someone who has leprosy. In the Middle Ages it spread across Europe. To protect the population, strict laws were enacted that banned the afflicted from all social contact. There was little treatment for the disease and no hope for a cure. Therefore, in addition to the physical suffering of their disease, there were the social stigmata of being “unclean” and “outcast”. In the 13th century, King Philip IV, of France, proposed a radical elimination of all people with Leprosy; gathering them in one place and burning them. As Leprosy declined in Europe by the 15th century, sailors and slaves carried it to the New World. It probably came to Hawaii by trading ships that had visited China. In 1865, King Kamehameha V, at the urging of the Christian population, segregated the Lepers to Kalawao, on the island of Molokai, a site backed by high cliffs and surrounded by the Pacific.12-14

On October 7, 1860 Joseph de Veuster, born in Tremeloo, Belgium, followed his older brother August into the Congregation of the Sacred Hearts of Jesus and Mary. He was twenty years old, and took the name Father Damien. In 1864 he arrived in Honolulu Hawaii. In 1866 the first 141 Lepers were taken to the Leprosarium on Molokai, where the conditions quickly became deplorable. A Priest visited once a year, but the priests requested a more frequent chance to help the Lepers. The Bishop Maigret, of Hawaii, granted this, and, at age 33, in 1873, Damien, at his own request, was transferred to the Leper Colony on Molokai island, where he was taken aboard the steamer Kilauea. The Bishop told the Lepers that Damien was “one who will be a father to you, and who loves you so much that he does not hesitate to become one of you; to live and die with you.”
While there he built 300 homes, built a pipeline for fresh water from a stream, buried the dead in coffins (estimated that he built 1600 coffins), instead of dumping their bodies into a ravine or allowing pigs to eat them. He bandaged their wounds and did their amputations. In 1885 it was clear that he had Leprosy. He labored until his death on April 15, 1889, by which time "his face had become terribly disfigured, his larynx and lungs infected, his hands and feet encrusted with sores." By the time of his death there were two other priests and an American lay worker, Joseph Dutton at Kalawao. In 1936 his body was transferred from Molokai to Antwerp. On June 4, 1995, Pope John Paul II beatified Father Joseph Damien de Veuster.\textsuperscript{12,13}

Locations where care is provided to Lepers now is a "Father Damien House."

\textbf{FATHER DAMIEN HOUSE; GUAYAQUIL, ECUADOR, 2004}

Front row, residents of Damien House; Back row, a medical mission group.
Gerhard Henrik Armauer Hansen was born July 29, 1841 in Bergen, Norway. After finishing medical school in 1868, he returned to Bergen, which was the center for Norwegian leprosy research. Leprosy was a social problem there, with 3000 Lepers, of whom 800 occupied hospital beds. It was believed to be inherited. He worked under Daniel Cornelius Danielssen, who had written a book “On Leprosy” in 1847. His studies of the patients, however, convinced him that there must be a specific cause. He postulated it was a bacteria, as he observed swollen lymph nodes in patients, but at that time, no human disease had been traced to a bacteria. He traveled throughout Europe learning histopathology and staining techniques. In 1871 he returned to Bergen. He identified rod-like structures in cells of cutaneous nodules, and published his 88 page paper in 1873, describing *Mycobacterium leprae*.

Armauer Hansen, MD
Bergen, Norway

His Drawing:
Schwann Cell/axon

His Original Stain
Red = *M. leprae*

LEPROSY IS NOW CALLED HANSEN'S DISEASE
Hansen was not convinced that this small intracellular rod was the pathogen, because he could not get it to infect animal models. He tried to infect his co-workers with injections, but failed. He tried then on a sicker host, a female patient with the neural form of Leprosy. He inoculated material drawn from a leprous nodule of a patient with cutaneous Leprosy into this woman's eye. While there were no clinical consequences of this, the patient claimed her sight was impaired, and brought criminal charges against him, leading to his removal as Director of Leprosarium No. 1. However he was permitted to stay as its Chief Medical Officer for Leprosy. This was the first description of a bacteria as a human pathogen, even though it failed what were later to be called Koch's Postulates. In 1876, just three years thereafter, Robert Koch demonstrated the transmissibility of anthrax. (It is this continued failure of *M. leprae* to be transmitted in an animal model that has prevented the formation of a vaccine for Leprosy.) Of historic interest, the bacteria that causes Tuberculosis was not described until 1882. Related to Hansen’s efforts, Norway passed the Leprosy Acts of 1877, and 1885, permitting health authorities to order Lepers to live in precautionary isolation away form their families, leading to the decline of Leprosy in Norway. He died February 12, 1912. His urn lies beneath a bust of him in the botanical gardens at the University of Bergen.  

The first use of an antibiotic for Leprosy was likely due to the efforts of a Scottish dermatologist, Robert Cochrane. He worked primarily at the Sanatorium at Chingleput, in Southeastern India, south of Chenai (formerly Madras). In 1924 he was appointed Medical Secretary to the Mission to Lepers, in which post he visited all the Leper Institutions in India and Burma, Malay, Borneo and the Phillipines. In 1935 he assumed the leadership of the Lady Willingdon Leprosarium in Chingleput. He was also
responsible for the Leprosy work in Vellore and Madras. The Sanatorium at Chingleput was run by the Church of Scotland. The concept there was not to house the lepers apart from the institution, but rather to create a model facility, a lovely, sprawling campus of neat yellow buildings with red tile roofs. Missionaries had planted long rows of mango and tamarind trees, and Chingleput stood out like an oasis in the rocky, red clay terrain of this region.

Typical Leprosarium
Champa, India, 1910

Robert Cochrane’s
Leprosy Survey of India, 1929

VIEWS OF CHINGLEPUT LEPROSARIUM
Dapsone (diamino diphenyl sulphone) was administered by Cochrane to the Lepers as an intramuscular injection with the drug dissolved in an oil. Dapsone is bacteriostatic. Over time it causes anemia. Dapsone became the main drug for the treatment of Leprosy for thirty years.\(^{20}\) Over the period from 1947 to 1964 he wrote three books on Leprosy.\(^{21-23}\) His work was carried on at the Leprosy Study Centre on Wimpole Street in London, and is now commemorated by the Robert Cochrane Fund for Leprosy, sponsored by the Royal Society of Tropical Medicine and Hygiene in London. He was President of the International Leprosy Association. In 1964 he won the Damien-Dutton Award. His son Ian H. Cochrane, MD, continued working with Leprosy in Bangladesh.\(^{17}\)

Another legacy left by Cochrane was his introduction of Paul Brand to the field of Leprosy. Brand finished his orthopedic surgery residency in England in 1946, and was destined for military service. At that point he met Cochrane, who knew of Brand’s parents’ missionary work in the \textit{Kolli Mallis} (literally mountains of death) in India, north of Chennai. Although Paul Brand was born to Christian missionaries in India in 1914, it was not until Cochrane induced him to come to India that Brand did return.\(^{24}\) His wife, Margaret, an ophthalmologist, with him.


Margaret and Paul Brand, MDs, circa 2002
Brand relates this story of his first observing his father interact with Lepers, he was about 8 years old (Appendix 4). When Cochrane brought Brand to Chingleput to visit the Lepers for the first time, Cochrane described the skin disorders in great detail, but Brand was struck by the hand and foot deformities. Brand had become interested in pain, due to his observations of pain in people in India during his childhood and because of inspiring teachers in England, such as Sherrington. Sherrington, a Noble Laureate in Neurophysiology called the brain the "enchanted loom", patterns of light flickering on and off. Brand had dissected cranial nerves with interest in medical school. Now he was fascinated with the patterns of facial palsy, corneal opacification, ectropion, and upper and lower extremity paralysis he saw in Leprosy. His review of the literature demonstrated nothing had been written in orthopedic journals about leprosy.

Examining Patients with Leprous Neuritis  

PAUL WILSON BRAND (1914-2003)

circa 1990
In 1936, the Nobel Prize in Medicine went to German pharmacologist Otto Loewi, who discovered, in frog muscle, the basic chain of chemical reactions that permitted nerve impulses. When Brand was in Medical School in Cardiff, Wales (1939, when Hitler invaded Poland), scientists at Woods Hole, Massachusetts and Plymouth, England first recorded electrical signals from the giant squid axon. Brand learned that when the ear detects a vibration, the vibration is not felt in the brain, but a signal is recorded there. Brand planned a dissection of the cranial nerves, not a required project:

“The mandibular branch of the very large fifth cranial nerve had presented a dissection challenge, for the nerve tunneled through the jawbone, emerging in numerous places to supply sensation for the lips and teeth. When I chiseled through bone and enamel to expose the slender axons in the teeth, I came across untreated dental cavities. I though back to childhood memories of blinding toothache pain; the Welshman’s nerve must have carried similar messages of torment. Yet that same nerve also carried subtle sensations from the lips; every pleasure from every kiss had traveled the identical pathway to the brain. Whatever its source in the head, tooth decay, scratched cornea, pierced eardrum, canker sore, pain travels along one of the twelve cranial nerves, and presents itself to the brain in a code identical to that used for conveying hearing, smell, vision, taste, and touch. How could the brain sort out such mixed messages? I came away from my dissection project awed by the economy and elegance of the system that transcribes the vast phenomena of the material world.”27
Brand began to record the pattern of hand and foot deformities, finally obtaining data on 2000 patients. From these he noted that:

“frequent paralysis in areas controlled by the ulnar nerve, moderate paralysis in the median nerve, and very little in the radial nerve. I could think of no logical reason why the ulnar nerve at the elbow would cause paralysis while the median nerve, one inch away, stayed healthy; or why the median nerve went dead at the wrist while none of the radial nerve muscles was paralyzed. To add to my confusion, I had sent tissue samples from shortened fingers to Vellore’s professor pathology. The reports came back as normal tissue, except for the loss of nerve endings.”²⁸

Images of deformity and disability in Leprosy patients in Ecuador, September 2004. *EACH OF THESE PATIENTS HAS HAD MDT and IS “FREE OF LEPROSY”!!*
Autopsy was considered by the Hindu's as mutilation, leaving the body unsuitable for re-incarnation, and, therefore, the dead bodies had to be burned. But one day, Brand's team had the opportunity, if done late at night, to dissect out the nerves from a dead Leper. "The setting, a silent moonlit light, the heat, the isolation in the jungle, a corpse full of germs, was worthy of a horror movie:

The body, an elderly man's showed evidence of severe deformity: claw-hands, shortened fingers and toes, facial deformities. He was a classic "burnt out case". The Leprosy bacteria had done all the damage they could do and then died out... On one side of the body, sections of the nerves were put into bottles and labeled, on the other side I dissected out the entire length of the nerves: I wanted to see the whole nerve in relation to the bones and muscles. Three of us worked for hours. The only sounds were the clicking of instruments and the high pitched wine of circadas, outside. We did the arms, the legs, the face... By the kerosene light, the dissected nerves, lying on the skin, gleamed white in contrast to the dark body. When I stood and looked, finally taking a break, I saw it. 'Look at the nerve swellings. Do you see a pattern?' At certain places, behind the ankle, just above the knee, and also at the wrist, the nerves swelled up to many times normal size. Swellings also bulged slightly on the facial nerve branches at the chin and cheekbone, and were most marked just above the elbow on the ulnar nerve... We saw clearly that nerve swellings tended to occur in just a few sites. Indeed, swellings arose only where the nerve lay close to the skin surface, and not in the deep tissues. For the first time I sensed some rationality behind the mystery of leprosy-induced paralysis."

Examples of massively swollen nerves, close to the skin, and just proximal to a joint:
Left: ulnar nerve, at elbow. Arrow at notch where Osborne's band has been released. Right: tibial nerve in tarsal tunnel, proximal to constriction in plantar tunnels.

In that autopsy, muscles controlled by nerves located deep in body tissue did not seem endangered, being red and normal bulk. In contrast, muscles controlled by nerves that passed close to the skin surface were pink and shriveled. This meant to Brand that he
could now identify forearm muscles for use in reconstructive surgery, possibly to transfer over to replace the paralyzed muscles, with no fear that they might become paralyzed by M. leprae later. Brand’s team was to learn that there was an explanation: to multiple, M. leprae liked cooler temperatures that prevail close to the surface, explaining why bacteria were found in large numbers in the testicles, earlobes, eyes, and nasal passages.

“The body’s immune system reacts with macrophages and lymphocytes which settle in the nerve’s sheath “choking off vital nourishment”. The swollen nodules along the nerves “represented the body’s own defense response to an invasion.” After that dissection, Brand’s team went to Robert Cochrane’s house for breakfast.”

“Leper Cured” by Ian Pollock, 2000
Brand began to publish his observations, but was met with obstacles to acceptance that exist to this day. It was believed that because Lepers had "bad flesh" they would not heal if elective surgery were done. It was believed that if people knew a traditional hospital was operating on Lepers, "regular" people would not come to that hospital. Even when it was proven that by protection of the anesthetic parts prevented loss of the anesthetic digits or nose, the physical stigmata of the hypopigmented skin, the missing eyebrows, and the signs of limb deformity prevented the Leper from achieving social acceptability. Lepers were treated with Dapsone, and were no longer contagious, but were still kept in Leprosariums, apart from society.

Brand taught himself how to do hand surgery, just as Bunnell, a general surgeon and gynecologist, taught himself hand surgery in order to help those injured hands he saw in war. Brand got Bunnell’s 1944 book on Hand Surgery, and from it studied the operations for tendon transfer that Bunnell had invented. Brand invented his own set of transfers for the Leprosy patients, and taught himself, and countless others thereafter, how to do that surgery and how to rehabilitate the patients.

When he left Vellore, he became in charge of the United States’ National Leprosarium in Carville. His obituary, with an accounting of his many honors, is given in Appendix 5. He died at the age of 89 in 2003.

On a personal note, Paul Brand influenced the Chief of Plastic Surgery where I went to medical school, as that Plastic Surgeon studied with him in Vellore. The techniques that Brand used in Carville to study sensibility in Leprosy became part of my research work in medical school, and continue to be used to this day. In 1977, Brand opened the Hand and Rehabilitation Center in my city. I am honored to be carrying on his work with Leprosy today, as illustrated in the photographs of the Leprosy patients from Ecuador included in this Essay for the Plastic Surgery Educational Foundation.
THE MEDICAL TREATMENT OF LEPROSY:
MULTIPLE DRUG THERAPY (MDT)

The is evidence from the Sushruta, 600 B.C., and from mention in the Bible, that Chaulmoogra Oil (sometimes called Hydnocarpus Oil) was taken orally to treat Leprosy. However, it is unlikely that this thick oil had any medicinal value. Dapsone, a bacteriostatic sulfa drug, was successful at stopping contagion from *M. leprae*, but drug resistance emerged. Lamprene (clofazamine), a drug that was partially bacteriocidal was introduced in the 1960’s, and in addition has anti-inflammatory properties. It is, however, a dye, and can color the cornea and the skin a darkish blue. Rifampin was introduced in the 1970’s. The combination of these three drugs was termed multiple drug therapy (MDT), and was proclaimed by the World Health Organization in 1981 as the official protocol for the medical treatment of Leprosy, with the goal of Eradication of Leprosy. At that time the world prevalence of Leprosy was about 15,000,000 people. For the paucibacillary form of Leprosy, which is the same as the Tuberculoid form, the protocol requires treatment for 6 months. For the multibacillary form of Leprosy, which is the same as the Lepromatous form, the protocol requires treatment for 24 months. Appendix 6 gives the typical treatment regimens in terms of drug doses and schedules. In 2003, the U.S. Food and Drug Administration approved the use of Thalidomide for the treatment of Erythema Nodosum Leprosum, a painful skin disorder that can occur during MDT. Thalidomide is indicated when Chloroquine, Aspirin, and Prednisone are not effective in its treatment.

Eliminating leprosy
Leprosy can be cured with MDT. It is highly effective. Patients with paucibacillary leprosy are cured in six months and those with multibacillary leprosy in twelve.

MDT kills the bacilli, and interrupts the transmission of leprosy. After the first dose of MDT, patients are no longer infectious.

MDT is a combination of two to three drugs: dapsone, rifampicin (Rimactane®) and clofazimine (Lamprène®). Through the combination of medicines, the development of resistance to treatment is prevented. MDT is the standard treatment recommended by the World Health Organization (WHO) since 1982.

The best way to prevent spread of leprosy is to treat all patients with MDT.

Through early cure, MDT prevents disabilities. WHO estimates that early detection and treatment with MDT have prevented disabilities in 3 to 4 million people. Given the extent of the economic and social loss which MDT prevents, curing leprosy can be considered to be highly cost-effective.

MDT is safe and effective. Patients can continue their treatment during pregnancy or while breast feeding. It is also safe for patients who are HIV- positive as well as those suffering from tuberculosis (TB).

There is virtually no recurrence of the disease after treatment has been completed. No resistance to MDT has been detected.

MDT is provided in blister packs each containing 4 weeks treatment. The blister packs facilitate patient compliance with the treatment, are easy to administer under field conditions and protect the drugs from heat and moisture.

Novartis provides WHO with adequate quantities of MDT, in blister packs, free of charge for the treatment of all the patients in the world.

Eliminating leprosy as a public health problem means bringing the disease burden down to a very low level. This will lead to a reduction in the source of infection, so that leprosy is likely to disappear naturally – as it already has in many parts of the world. WHO has defined “elimination” as a prevalence rate of less than 1 case per 10,000 people.

Leprosy will be “eliminated” when we detect all those suffering from the disease and cure them by using multidrug therapy (MDT).

The large-scale use of MDT has reduced the disease burden dramatically. Over the last two decades over 13 million people have been cured of leprosy. The prevalence rate of the disease has dropped by 90% from 21.1 per 10,000 inhabitants to less than 0.8 per 10,000 in 2004.

Today leprosy is a public health problem in only 9 countries - compared to 122 countries in 1985.

toptop Eliminating leprosy
toptop Eliminating leprosy

toptop Eliminating leprosy

toptop Eliminating leprosy

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toptop Eliminating leprosy
LEPROSY TODAY IN THE UNITED STATES OF AMERICA

Well yes, I have seen and operated upon one patient with Leprosy in the United States. He was referred to me to close an ulcer behind the left ear, caused by his eyeglasses. He claimed a history of the rare “congenital insensitivity to pain”, his neurologist had told him he was born without “C-fibers”. Of course, I knew of this rare disease, but had never met someone with this. His ulcer was easily excised, and then closed with a retroauricular flap. The pathology report indicated chronic ulceration, without evidence of cancer. The following year a dermatologist in my city called me with a follow-up. The patient had consulted him because of eyebrow hair loss. The dermatologist entered (anesthesia + hair loss) into his PDA and came with only one diagnosis: Leprosy! A review of the ulcer I had excised, when now stained for acid-fast bacteria, demonstrated M. leprae, and he had begun MDT. Upon further questioning, the man, who was a wine steward, a Sommelier, had traveled extensively throughout the world pursuing and tasting great wines. That was in 1992.

And so it is with most of the 200 cases of Leprosy now reported per year in the U.S.A. Today there are 6000 patients with Leprosy in the United States, with 95% of these patients acquiring their disease in developing countries.\(^{46,47}\) For example, May 2, 2003, the National Hansen Disease Program reported 110 new cases, from 27 states and Puerto Rico; six states (Texas, New York, Louisiana, Washington, Florida, and California) accounted for 71% of the total number of cases reported. It has been conjectured that many of the new cases of Leprosy in the United States are illegal alien immigrants from Mexico, Brazil, the Caribbean and India. These people are often hired into food service, dish washing, cooking, hotels, and day care, so that Leprosy can spread across the country. Two people in New York City area in 2004 were identified who had no history of foreign travel, suggesting that there may now be an endemic region in the Northeastern part of the United States.\(^{49}\)

The well-known and accepted area of the United States is where the Gulf of Mexico touches Louisiana and Texas. It is this area where the National Leprosarium is located in Carville, Louisiana, the location in which Paul Brand, MD worked for so many years. It has been reported that this hospital is being “phased out” \(^{50}\)
The only known animal reservoir for M. leprae in the United States is the 9-banded Armadillo (*Dasypus novemcinctus*). This animal is in Texas. This is a New World animal, found only in the Western Hemisphere. The disease has been identified in Armadillos in Argentina, Brazil, and Mexico.

In 1985, The World Health Organization reported the prevalence of Leprosy to be 12 million people. In January of 2003, the number of people in treatment (MDT) for Leprosy was estimated to be 534,000, as reported by 110 countries. In 2002, about 621,000 new cases of Leprosy were detected. Worldwide today, the prevalence of Leprosy is reported to be 5.5 million people. Eighty percent of these cases live in the tropics and subtropics: India, Myanmar (Burma), Nepal, Indonesia, Bangladesh, Brazil, Madagascar, Mozambique, Tanzania and Nigeria. Every hour 65 new cases of Leprosy are detected and 11 of these are children.\(^{51,52}\)

**ELIMINATION OF LEPROSY IS NOT ERADICATION:**

**ELIMINATION OF CONTAGION DOES NOT PREVENT PROGRESSION OF DEFORMITY AND DISABILITY.**\(^{53}\)

This paradox has been beautifully expounded and is given in Appendix 8. In essence, despite MDT dropping the prevalence of Leprosy from 12 per 10,000 to 1 per 10,000 population (the W.H.O. definition of “elimination”), half a million new cases occur per year and the chronic problems relating to the progressive neurologic disease continues despite MDT preventing contagion and having a relapse rate of just 1\%.
PLASTIC SURGERY AND LEPROSY

Within ten years of Paul Brand introducing Leprosy to the surgical literature, Plastic Surgery leaders like Noshia Antia, in Bombay, India, Fritischi, in London, Engloand, and Frank McDowell, in Honolulu, Hawaii, U.S.A were writing about reconstruction of the Leper. The Sushruta, from 600 B.C. describes nasal reconstruction, and so it is not surprising that this prominent feature was among the first aspects of deformity that was approached by Plastic Surgeons. The unique and challenging features of the nose are such that after 40 years of work by Plastic Surgeons in this area, the most recent paper by a Plastic Surgeon on Leprosy is about nasal reconstruction in Leprosy, from April of 2004.

According to the classification of Schwarz and Macdonald, the above patient would be classified as having a mild nasal collapse, characterized by septal destruction with a small perforation, and would be best reconstructed with cartilage grafts. In the patient with a moderate degree of collapse, characterized by both septal and bone destruction, has more
obvious nasal collapse, like the patient pictured below. For moderate degree of nasal
collapse, if mucosal lining is sufficient, cartilage and bone grafting is required, and if
lining is insufficient, then nasolabial flaps or mucosal inlay grafting is required.⁶¹

For the severe degree of nasal collapse, in which there is skin tethering related to
secondary infection, additional skin, provided by a forehead flap is necessary.⁶¹ With this
algorithm, among 49 patients, with a mean follow-up of 23 months, there was an 83%
good to excellent cosmetic result. This series of patients had Leprosy a mean of 18.6
years with a mean history of nasal collapse of 7.5 years. When the cosmetic result is
subdivided based upon degree of severity of the nasal collapse, as might be predicted,
there were 80% excellent results in the mild degree, 22% in the moderate degree, and
16% in the severe degree of nasal collapse.⁶¹

Another area to attract early attention of Plastic Surgeons was facial palsy. In
1966, Antia described branches of the facial nerve being affected by Leprosy where they
exited the parotid fascia.⁶² The primary concern with facial palsy was corneal exposure, a
problem worsened by the fact that the M. leprae destroyed the fine trigeminal nerve
fibers that supplied sensation to the face and cornea. Tarsorrhaphy was the procedure of
choice for correction of lagophthalmos. Fritsch observed the greatest laxity was on the
medial half of the lower lid\textsuperscript{57} and so the medial tarsorrhaphy became preferred in the treatment of Leprosy, in contrast to the lateral tarsorrhaphy (arrow) below.\textsuperscript{41} The medial tarsorrhaphy has the added advantage of turning in the medial lacrimal punctum.

![Image of a patient's eye with an arrow pointing to the medial lacrimal punctum]

Face lifting in the patient with Leprosy has been described, but has not been well documented.\textsuperscript{41} The temporalis transfer for orbital closure has been done successfully in the Leper,\textsuperscript{41} with the narrowing of the eyelids being considered a virtue rather than a drawback as it affords corneal protection. The question of whether cross-facial nerve grafting or an innervated microsurgical transfer would be helpful in Leprosy depends upon whether the target tissue, facial muscle, can still be re-innervated and whether or not the proximal unilateral facial nerve has been destroyed by \textit{M. leprae}. The most recent study on this suggests that just the distribution of damage is variable; of three patients, one had only the zygomaticotemporal branch of VII destroyed, but in two patients, even the trunk of VII was destroyed. In that study, however, regenerating unmyelinated fibers were identified by electron microscopy, indicating that there is some hope for distal re-innervation.\textsuperscript{63}
Reconstruction of foot ulceration has long been of interest to Plastic Surgeons in patients with Leprosy. Paul Brand developed and reported on non-operative approaches to treat these problems, ranging from foot protection for prevention, to a form of what we would now call contact casting. The range of flaps used for reconstruction of the foot ranged from the local flap to the cross-leg flap. A local flap that has considerable value is the innervated dorsalis pedis flap, as this would carry with it sensibility, since the deep peroneal nerve may be spared from \textit{M.leprae}. This flap was reported to be used successfully with a 36 to 120 month follow-up in 30 patients with Leprosy, with just one recurrence. The volar-innervated, 1st/2nd toe webspace flap has been reported to be used successfully with a 12 month follow-up in 16 patients with Leprosy, with just one recurrence, which was felt to be due to dehiscence.

A recent outcome study of healing in 2599 foot ulcers in 1804 Leprosy patients from China was reported in 2003. Flaps were not used for these patients. Overall, 56% of the ulcers healed. Those treated in the Leprosy hospitals had a cure rate of 71%, with a 15% recurrence rate, in contrast to those who lived at home, who had the lower cure rate, and a recurrence rate of 18.4%. It therefore appears that when the surgical ability is available, closure of foot ulceration with a regional innervated flap provides the best alternative for long-term healing.
Can the Plastic Surgeon be involved in the surgical treatment of pain? Paul Brand's primary approach was to recognize that the absence of pain was the cause of anesthesia, and unprotected skin with anesthesia will result in digital loss in the hand and foot. But anesthesia represents the end stage of the peripheral nerve problem. With increasing frequency, it is now being recognized and written: neuropathic pain is part of the overall problem in Leprosy.\textsuperscript{68-73} Acute pain in one or several nerves may be the presenting feature in Leprosy, due either to entrapment of enflamed, swollen nerves or "reversal reactions" to the MDT. The dynamic state of the immune response to \textit{M. leprae} leads to spontaneous fluctuations in the clinical state, or "reactions". Type 1 reaction or reversal reaction is caused by spontaneous increases in T-cell reactivity to antigens,\textsuperscript{74} especially in those patients with Borderline or Tuberculoid Leprosy.\textsuperscript{75} Type 2 reactions, or Erythema Nodosum Leprosum, is a systemic inflammatory response to the deposition of immune complexes, in Borderline or Lepromatous Leprosy.\textsuperscript{76}

Type I Leprosy Reaction at the elbow. Note swollen, purple ulnar nerve.
Type II Leprosy Reaction; Erythema Nodosum, due to Ag-Ab complex deposition.

The management of the painful Type II reaction requires systemic medication because it is a systemic reaction; prolonged high dose steroids are required usually,\textsuperscript{76} and the patients may be toxic, with high fevers, joint and gastrointestinal involvement. For Type I painful reactions, surgical decompression of acute nerve compression, as noted above for the cubital tunnel is effective. And decompression of peripheral nerves for painful thickened nerve trunks, where they may be an abscess is helpful for pain, too.

Peroneal Nerve at knee decompressed for \textit{Abscess}. Note wrinkled skin and orange color of fat, which are complications of Rifampin.
PERIPHERAL NERVE SURGERY AND LEPROSY:

HISTORIC REVIEW

It has been difficult to identify the first peripheral nerve surgery done for Leprosy. For example, in Brandt encyclopedic chapter on rehabilitation in leprosy,\(^4\) he has the following pessimistic (relatively uncharacteristic for him) statements:

"There are two major indications for operating on nerves in Leprosy. The first is to preserve or restore function. The second is to relieve pain. No operation can prevent or correct the segmental demyelination that is the direct result of the activity of \(M.\ leprae\)... It is generally accepted, even by the most enthusiastic surgeons, that neurolysis has no place in the treatment of common peroneal paralysis."

Brand's indication for peripheral nerve decompression is 1) repetitive sensorimotor clinical exam documents loss of peripheral nerve function, 2) no response of peripheral nerve to full course of steroids, 3) peripheral nerve function continues to deteriorate.\(^4\)

For the ulnar nerve at the elbow, the surgery would include an external neurolysis but without disrupting its blood supply, opening any constriction, excising a portion of the medial humeral epicondyle if it were too tight, "lift off" the epineurium over \(1/3\) to \(1/2\) the circumference of the nerve, and if an abscess is identified to excise that segment of nerve.

With regard to the carpal tunnel, Brand said, "the median nerve rarely has a thick sheath and is not often improved by surgery. The release of the carpal tunnel may be helpful when the nerve is swollen."\(^4\) "The tibial nerve may be exposed behind the ankle and freed up and down for a few centimeters, with incision of its sheath. This has proved to be a benefit when pain persists or loss of sensation is progressive."\(^4\)
Brand cautions about interpreting pain relief as functional improvement:

"Medical relief is slow. Surgical relief is immediate and the patient is so grateful that he or she willingly and enthusiastically reports that everything has improved, sensation, motor power, range of motion of joints. Only when strictly objective testing is carried out in a double blind trial does it become apparent that sometimes sensation and motor power have not been affected, or even that they may have regressed."\(^{41}\)

While current medical reports do not mention a surgical approach for peripheral nerve problems,\(^{74,76,77}\) there is a small body of literature related to peripheral nerve surgery in Leprosy. A few reports of nerve grafting for irreparable damage to the ulnar nerve, usually in the presence of abscess, was reported in the late 1970's, shortly after Millessi introduced interfascicular interposition nerve grafting. Nerve graft results did not give improved function.\(^{78-80}\) However, there are many reports of decompression of the ulnar nerve at the elbow for the treatment of pain, utilizing the whole spectrum of reported procedures with the exception of submuscular transposition.\(^{81-86}\) In general, these studies have reported significant pain relief, with some improvement in sensation and some improvement in motor function. The claim is made the deformity is prevented when the nerve decompression is done in early cases. It is noted the electrophysiological tests do not recover to more than 80% of normal function, and often much less, even when there is good clinical and symptomatic improvement.\(^{86}\) Much less has been written about carpal tunnel decompression for the median nerve; In the one paper devoted just to this nerve, of 29 patients who had a decompression, sensory recovery was seen in 90% of cases, and in 45% muscle strength improved, while in another 25% motor function had no further deterioration.\(^{8}\)

Median nerve decompression is also commented upon in one of the studies reporting ulnar nerve results.\(^{85}\) Where the degree of nerve compression was graded pre-
operatively and clinically staged, of 3 patients with moderate degree of compression, only one patient improved, and two had no change, in contrast to 6 patients with severe compression, of whom 3 recovered normal strength and improved sensation, 2 cases were worse, and one was not improved. When median nerve post-operative results are compared to those following cubital tunnel decompression using this same staging paradigm, for the moderate degree of ulnar nerve compression, of 15 patients, 4 were better and 11 were not improved. For the severe degree of compression, of 17 patients, 6 were better, 5 were without change, and 6 were worse. Husain, et al’s results for the ulnar decompression, were also, in the same area of success, although they did not clinically stage their patients degree of compression; while 49% had relief of pain, 11% failed to improve in terms of sensory or motor recovery, and those who had some degree of improvement were combined with those who “were prevented from getting worse to give the appearance that 89% of patients were benefited by the ulnar nerve surgery.

Pandya’s report, in addition to including carpal and cubital tunnel decompression, did also include tarsal tunnel decompression and neurolysis of the common peroneal nerve. There are three other brief reports on tarsal tunnel surgery. One, using sweat production as a functional outcome measure, reported an improvement following a traditional posterior tibial nerve decompression, the second one, added an internal neurolysis of the posterior tibial nerve and a sympathectomy to restore sensation and improve ulcer healing in a single patient, the third, written in French in 1976, suggests a role for neurolysis of the tibial nerve in patients with leprosy and diabetes.

With regard to Paul Brand’s indication for peripheral nerve surgery requiring a course of steroids, it is interesting to look at two of the most scientifically designed
studies related to the treatment of peripheral nerve problems in Leprosy. In 1996, for the treatment of “early ulnar neuritis”, a randomized trial of ulnar neurolysis combined with medial epicondylectomy was compared to full course of high dose steroids. There were about 20 patients in each group, and they were followed for two years. There was no difference in the outcomes between the two groups. In 2003, a multi-centered, randomized, double-blind, placebo-controlled trial was conducted in Nepal and Bangladesh, with one group getting either high dose prednisolone, tapered over four months, versus one group receiving a placebo. In this study, patients had a higher degree of nerve function impairment (NFI) then in the previous study, with duration of NFI ranging from 6 to 24 months. Of 92 patients followed for one year, “no demonstrable additional improvement in nerve function, or in preventing further leprosy reaction events was seen in the prednisolone group. Overall, improvement of nerve function at 12 months was seen in about 50% of patients in both groups. This result was the same for the ulnar nerve and for the posterior tibial nerve. Leprosy reactions and new NFI occurred in a third of the group, emphasizing the need to keep patients under regular surveillance during MDT, and where possible, after completion of MDT.”

Summarizing the diverse, retrospective case studies in the surgical literature on Leprosy from the past 25 years, a systematic review, one can only infer that traditional decompression surgery can relieve pain often, improve function in less than 50%, and has the potential to result in even worse peripheral nerve function. With regard to the only two, high level evidence-based studies, one could summarize by saying that, for the ulnar nerve at the elbow, giving steroids gave no better results than doing surgery, and steroids gave no better results than doing nothing, and therefore, by inference, there is no demonstrated value in doing surgery in terms of functional improvement! This is a difficult conclusion for a Plastic Surgeon to accept. Could there be another surgical approach, based upon a 21st century understanding of peripheral nerve function.
OPTIMISM FOR FUNCTIONAL IMPROVEMENT:
DECOMPRESSION OF MULTIPLE PERIPHERAL NERVES, SIMULTANEOUSLY, IN LEPROSY

Three recent streams of knowledge are now converging to create the environment for an advance in functional improvement of both the upper and lower extremity in Leprosy through peripheral nerve surgery, an area in which Plastic Surgery can exert a creative leadership.

The first area involves a series of epidemiologic studies that have demonstrated collectively, by using the World Health Organization's definition of Nerve Function Impairment (NFI), and correlating it with measurement of sensibility by health care workers in the field, that at the time of diagnosis of Leprosy, approximately half of the people have a NFI, but that virtually all have some degree of sensory impairment in either upper or lower extremity or both.93-99 These studies have utilized "instruments" for neurosensory testing of Leprosy that include nylon monofilaments, and ball point pens, and have included a definition of abnormal or protective sensibility that would be indicative of severe axonal loss if newer computer-assisted neurosensory testing were utilized for the foot.100

The second area involves the pathophysiology of M. leprae, which may now best be understood to involve entry of bacteria into host blood stream via mucous membrane, attachment of bacteria to the laminin of peripheral nerves in cooler temperature locations, intraneural reactions related to underlying host immune competence, and progressive fibrosis of the peripheral nerve associated with persistence of neural regeneration.101-104
These studies demonstrate that the physical examination demonstrating thickened nerve trunks or abnormal sensibility does correlate with skin and nerve invasion by *M. leprae*, and that once the infection has been treated by multidrug therapy the intraneural pathology remains as the basis for the progressive deformity and disability.

The third area involves the molecular biology of a bacterial rod:

**THE DOMAIN OF THE GLOB:**

**ADHESION OF ROD TO HELIX**

Laminin structure and laminin-binding integrins.

*(The G2 Domain of the alpha 2 chain of laminin will bind to *M. leprae)*

Laminins are αβγ heterotrimeric proteins. The N-terminal globular domains of the β and γ chains are important in laminin polymerization; in addition, two main integrin-binding regions have been mapped to (1) the N-terminal globular domain of the α1-chain short arm (integrins α1β1 and α2β1) and (2) the globular domains (G1, G2) of the α1-chain long arm. Schematic representation of the four best-characterized laminins – laminin-1, -2, -5 and -10 – and identification of corresponding preferential integrins.
Mechanisms of nerve invasion by *Mycobacterium leprae*:

Identifying the molecular basis of Mycobacterium leprae neurotropism is a high point in recent leprosy research. The G domain of the alpha2 chain of endoneurial laminin is crucial in the invasion of peripheral nerves by *M. leprae*. Alpha-dystroglycan has been identified as the laminin alpha2-G receptor on the Schwann cell and a candidate protein receptor on the surface of *M. leprae*. This work is a profound contribution to our understanding of the pathogenesis of leprosy and may have important implications for the design of interventions to control leprosy-induced nerve damage.\(^{106}\)

Identifying laminin alpha2 as the bridging molecule and alpha-dystroglycan as the receptor on the nerve, leaves the question, how is *M. leprae* binding to laminin? Using binding of radiolabelled laminin to *M. leprae*, the investigators identified a single cell wall protein of 21kDa, which appears to be the major adhesin of *M. leprae* for the interaction with peripheral nerve.\(^{107,108}\) The ends of the coiled triple helix structure bind to Type IV collagen. The grey side parts bind to other laminin molecules.
PLASTIC SURGERY STRATEGY for LEPROSY:  
APPLICATION in GUAYAQUIL, ECUADOR, 2004

In July of 2004, the Project Perfect World Foundation sponsored the first of two medical missions to evaluate the role of peripheral nerve surgery applications to patients with Leprosy. A Podiatric Foot and Ankle Surgeon, who had been going to this region to work on club foot problems, learned of the Fundacion Padre Damien in Guayaquil, Ecuador, whose Director is Sister Ann Credidio, BVM. A review article in the foot and ankle literature in June of 2004 demonstrated the basis for applying the concept of the double crush theory and the technique of decompression of multiple peripheral nerves to diabetic neuropathy. Could this approach help patients with Leprous neuropathy? The goal of the first mission was to identify potential patients for the surgery. The medical director of the Damien House, Pedro Martinez, MD, identified 51 inhabitants who were more than 6 months following their MDT, so they were no longer contagious.
Each patient had either upper or lower extremity pain, numbness, weakness and/or deformity, and was not having a Type II (erythema nodosum leprosum, i.e., systemic toxic) Reaction. The patients were examined for the presence of positive Tinel signs at known sites of entrapment, or tender, thickened peripheral nerves. Each had non-invasive neurosensory testing with the Pressure-Specified Sensory Device™ to document their degree of peripheral nerve impairment. Appendix 9 gives the distribution of the 120 nerves measured and the analysis in terms of the degree of peripheral nerve dysfunction identified in these patients. Based upon these evaluations, 26 patients were identified as potential surgical candidates for the second mission. That mission arrived in Guayaquil in September of 2004, and included two surgeons and a support team.
SURGICAL STRATEGY: Given that excellent surgeons had attempted to decompress nerves in patients with Leprosy in the past, what could we add to improve the chance of success? The double crush concept applied to Leprosy suggested that the host response to M. leprae occurred at locations where the nerve was superficial and where there were known sites of nerve compression. The conclusion was to decompress each nerve at each site in which it could be decompressed in that extremity. For the ulnar nerve, the decompression had to be at the elbow and at the wrist, and the decompression at the wrist had to include the motor branch of the ulnar nerve.

Clamp demonstrates the hypertrophic ulnar motor branch after incising the hypothenar muscle fascia at the hook of the hamate. Carpal tunnel opened.

For the median nerve, the decompression had to be at the wrist, and also, if possible in the forearm. In the absence of specifically finding evidence of the pronator syndrome, the approach used to the ulnar nerve decompression, the submuscular
transposition by the musculofascial lengthening technique, demonstrating the best long-term results, would decompress the median nerve at the elbow by lengthening the superficial head of the pronator and incising the lacertus fibrosus.

(left) Musculofascial technique for submuscular transposition of ulnar nerve at elbow: at this stage, the muscle flaps have been created, and ulnar nerve lies above, on muscle. (right) Muscle flaps transposed and lengthen, permit finger and ulnar nerve to lie beneath.

Radial nerve at the elbow lies deep to muscles, and would likely not be invaded by *M. leprae*, but superficial sensory branch should be decompressed in the forearm.

Hand is to the right. Elbow is to the left.

Note proximal normal size of nerve, and distally, at exit From fascia, the Enlargement of nerve, and site of Entrapment (arrow)

Neurolysis of the radial sensory nerve in the forearm. Fascia has been divided.
For the tibial nerve, its branches in the medial and lateral plantar and calcaneal tunnels would also be decompressed.

(Left) Posterior tibial nerve and its plantar branches released, with excision of septum between medial and lateral plantar tunnels to create one large tunnel. Note surgeon's finger extending into the plantar aspect of the foot.

(Right) Internal neurolysis of medial and lateral plantar nerves within tarsal tunnel.

For the peroneal nerve, it would be decompressed at both the fibular neck and over the dorsum of the foot.

For each patient, one upper and one lower extremity would be decompressed simultaneously, using a two team approach, under general anesthesia. Pneumatic tourniquets, bipolar coagulators, and 3.5x loupe magnification were utilized.
Internal neurolysis was done as indicated, based upon intra-operative findings of firmness, intraneural fibrosis, and loss of perineurial markings.

(left) Hypertrophic, firm right median nerve after division of transverse carpal ligament.

(right) Excision of epineurium and intraneural neurolysis of median nerve.

(left) Ulnar nerve in cubital tunnel, left arm. Nerve is diffusely firm.

(right) Excision of epineurium and intraneural neurolysis of the ulnar nerve.
**SURGICAL RESULTS:**

Nine patients had the above surgical approach, with surgical decompression of three nerves in an arm and three nerves in a leg done simultaneously. They each received intravenous cephalosporin prior to inflating the tourniquets, and they continued oral cephalosporin for one week post-operatively. There were no surgical complications. There were no anesthesia complications. As indicated from Appendix 9, there was a wide range of impairment pre-operatively in these patients. They were each kept the first night in the hospital, and were returned to the Damien House the day after the surgery. On examining them the day after surgery, many, who did not have fixed joint deformities in the hand (clawing) could already straighten their fingers and make a better fist. One patient is shown as an example of early recovery of sensibility in the foot after extensive neurolysis of the posterior tibial nerve and its branches.

Patient smiling one day (24 hours) after neurolysis of the tibial nerve and its branches in the four medial ankle tunnels. He had severe sensory loss prior to surgery. Note his smile as the sensory stimulus to the bottom of the foot now tickles.
Another patient is shown as an example of early recovery of peroneal nerve function after neurolysis, when there is not a long-standing, complete foot drop:

Neurolysis of the left common peroneal nerve at the knee. Note slightly inflamed and flattened common peroneal nerve. Nerve is not fibrotic. Peroneus longus fascia has been incised and fibrous band deep to the peroneus longus has been released.

(left) immediately pre-op; inability to extend big toe and dorsiflex ankle.

(right) immediately post-op, after neurolysis of common peroneal nerve at the knee; Note ability now to extend big toe and dorsiflex the ankle.
The mid-November 2004, 2 month follow-up was remarkable for no wound infections. Two patients who lived far away were not back for follow-up. Of the remaining ten patients, 7 said they had better sensation in the hand and foot that were operated on then they had before surgery, and they had better feeling in these operated extremities than they did in the non-operated extremities. Three patients noted no improvement. No patient was worse. The results were recorded by Dr Martinez, and submitted by email in the form of a chart for each patient by email. Appendix 10.

The mid-January 2005, 4 month follow-up was remarkable for continued improvement in sensibility and strength. One patient appeared to have his leg get worse, but then had a seizure and was found to have a brain metastasis (Appendix 10). An example of the four month report is given below:

<table>
<thead>
<tr>
<th>Jan, 12/05</th>
<th>R-Hand: Right now he can feel the presence of close hot objects or if bitten by a mosquito. Can use tools for agriculture (like a machete) hand has more strength. Does not have pain as before. Index and small fingers feel better. Generally feels better in relation to the left hand.</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td><img src="image" alt="Open and extended" /> <img src="image" alt="Open and together" /></td>
</tr>
<tr>
<td>L-Foot:</td>
<td>improvement in sensitive on plantar surface, much better than right foot. Also has improvement in strength of big toe and recovering sensitivity in lower leg.</td>
</tr>
</tbody>
</table>

Overall, of the 12 patients, 6 are in the excellent category, 4 are in the good category, with just 2 patients not improved. No one is worse. Below is an example of the
improvement in clawing that was accomplished in one patient so far who has been compliant with post-operative stretching of non-contracted PIP joints:

Jan, 21/05  R-Hand: has improved in the little finger and ring finger, has more strength in the hand and can write better. Sensitivity in index finger and plantar surface has improved, now can feel pain and the presence of near heat. Before regaining strength, the lower arm was inflamed. Now there is no inflammation or pain.

Open and extended  Open and together  Pinch

Jan, 28/05  R-Hand: photo of his hand after the therapy

REVERSAL OF CLAWING

IT IS HOPED THAT IN JULY, 2005, FOR THE 10 MONTH POST-
OPERATIVE FOLLOW-UP THE TEAM WILL RETURN TO GUAYAQUIL.
REPEAT NEUROSENSORY TESTING WILL BE OBTAINED TO HAVE
QUANTITATIVE DATA FOR COMPARISON OF SENSORY RECOVERY. A
DIFFERENT PLASTIC SURGEON FROM THE ONE INVOLVED IN THE
SURGERY WILL BE A MEMBER OF THE TEAM FOR AN UNBIASED
ASSESSMENT AND EXAMINATION OF THE EXTREMITIES.

IT APPEARS THAT THE PLASTIC SURGERY APPROACH
UTILIZED IN THIS GROUP OF PATIENTS WITH LEPROSY WILL
BE SUCCESSFUL. PERHAPS THE BIBLICAL CURSE WILL END.
APPENDIX 1.

HYSSOP

The content of essential oil is rather low (0.3 to 0.9%); it is mostly composed of cineol, β-pinene and a variety of bicyclic monoterpene derivatives (L-pinocamphene, isopinocamphone, pinocarvone). As many other plant of the mint family, hyssop contains rather large amounts of bitter and antioxidative tannines: Phenols with a diterpenoid skeleton (carnosol, carnosolic acid), depsides of caffeic acid (= 3,4-dihydroxy-cinnamic acid) and several triterpenoid acids (ursolic and oleanolic acid). Very similar or the same compounds have also been found in sage and rosemary.\(^4\)

A plant which is referred to in a few passages of Holy Writ. Its existence in Egypt is proved by Ex., xii, 22, wherein Moses is represented as bidding the elders of Israel to take a bunch of hyssop and to sprinkle with it the blood of the paschal lamb upon the lintel and the side posts of the doors of their dwellings. In the wilderness hyssop was also ready at hand, as can be inferred from Ex., xxiv, 8, completed by Heb., ix, 19, according to which Israel's great lawgiver sprinkled the Hebrews with hyssop dipped in the blood of victims, at the sealing of the old covenant between Yahweh and His people. The references to hyssop contained in the Mosaic ritual show clearly that it was a common plant in the peninsula of Sinai and in the land of Chanaan, and disclose its principal uses among the Hebrews. Thus, it is with hyssop that the blood of a bird offered in sacrifice is to be sprinkled for the cleansing of a man or a house affected with leprosy (Lev., xiv, 4-7, 49-51); it is with it, too, that the sprinkling of the water of purification must be made at the cleansing of a tent, a person, or a vessel polluted by the touch of a dead body (Num., xix, 8). Besides being thus used as an instrument in the act of sprinkling, hyssop was employed as one of the elements to be burned in the preparation of the water of purification itself (Num., xix, 6). It is not therefore surprising to find that this manifold and intimate connexion of hyssop with the various purifications of the Old Law led the Psalmist (Ps. 1 [Heb. li] 9) to regard the sprinkling with hyssop as symbolical of a thorough purification of the heart, a view which the Catholic Church has made her own in the ceremony of the Asperges which usually begins the solemn offering of Holy Mass. Nor is it surprising to find that this same connection of hyssop with the various cleansings of the Mosaic Law suggested to many writers the identification of that plant with the Hyssopus officinalis, or common hyssop, with which they were particularly acquainted, and the detergent properties of which they not unnaturally thought had induced the Hebrew legislator to select it as especially fit for the purificatory services in Israel. The plant, which at the present day, is considered as more probably the hyssop of the Mosaic ritual, is the Origanum maru. Like the Hyssopus officinalis it belongs to the family of the labiæ, has aromatic and detergent properties, and can be easily made into a bunch for purposes of sprinkling. Origanum maru grows on the walls of all the terraces throughout Palestine and Syria. This last claim in favour of the identification of the hyssop of the Old Testament with the Origanum maru, is in distinct harmony with III Kings, iv, 33 (Heb. I Kings, iv, 33) where we read that Solomon "treated about trees from the cedar that is in Libanus, unto the hyssop that cometh out of the wall".\(^5\)
APPENDIX 2.

NAAMAN<sup>6,7</sup>

1. Now Naaman, captain of the host of the king of Syria, was a great man with his master, and honourable, because by him the Lord had given deliverance unto Syria; he was also a might man in valour, <i>but he was a leper</i>.

2. And the Syrians had gone out by companies, and had brought away captive out of the land of Israel a little maid; and she waited on Naamans’s wife.

3. And she said unto her mistress, Would God my lord were with the prophet that is in Samaria: for he would recover him of his leprosy.

4. And one went in, and told his lord, saying......

9. So Naaman camae with his horses and with his chariot, and stood at the door of the house of Elisha.

10. And Elisha sent a messenger unto him saying, Go and wash in Jordan seven times and thy flesh shall come again to thee, and thou shalt be clean.

14. Then went he down, and dipped himself seven times in the Jordan, according to the saying of the man of God.; and his flesh came again like unto the flesh of a little child, and he was lean.

15. And he returned to the man of God, he and all his company, and came, and stood before him; and he said, Behold now I know that there is no God in all the earth but in Israel; now therefore, I pray thee, take a blessing of thy servant.

24. And Naaman said, be content take two talents. And he urged him, and bound two talents of silver in two bags, with two changes of garments, and laid them upon two of his servants; and they wore them before him.

25. And when he came to the tower, he took them from their hand, and bestowed them in the house, and he let the men go, and they departed.

26. But he went in, and stood before his master. And Elisha said unto him. Wence comest thou Gehazi? And he said thy servent went no whither.

26. And he said unto him. Went not mine hear with thee, when the man turned again from his chariot to meet thee? Is it a time to receive money, and to receive garments, and olive-yards, and vineyards, and sheep and oxen, and men servants, and maidservant?

27. The leprosy therefore of Naaman shall cleave unto thee, and unto they seed for ever. And he went out from his presence a leper as white as snow.
APPENDIX 3.

MIRIAM⁸

1. And Miriam and Aaron spake against Moses because of the Ethiopian woman whom he had married; for he had married an Ethiopian woman.
2. And they said, Hath the Lord indeed spoken only by Moses? Hath he not spoken also by us? And the Lord heard it.

5. And the Lord came down in the pillar of the cloud, and stood in the door of the tabernacle, and called Aaron and Miriam; and they both came forth.
6. And he said; Hear now my words; If there be a prophet among you, I the Lord will make myself known unto him in a vision, and will speak unto him in a dream.
7. My servant Moses, is not so, who is faithful in all mine house.
8. With him will I speak mouth to mouth, even apparently, and not in the dark speeches; and the similitude of the Lord shall behold wheretofore then were ye not afraid to speak against my servant Moses?
9. And the anger of the Lord was kindled against them; and he departed.
10. And the cloud departed from off the tabernacle; and behold, Miriam became leprous, white as snow; and Aaron looked upon Miriam, and behold, she was leprous.
11. And Aaron said unto Moses, Alas, my lord, I beseech thee, lay not the sin upon us wherein we have done foolishly, and wherin we have sinned,
12. Let her not be as one dead, of whom the flesh is half consumed, when he cometh out of his mothers womb.
13. And Moses cried unto the Lord saying, Heal her now, O God, I beseech thee.
14. And the Lord said unto Moses, If her father had but spit in her face, should she not be ashamed seven days? Let her be shut out from the camp seven days, and after that let her be received in again.
15. And Miriam was shut out from the camp seven days. And the people journeyed not till Miriam was brought in again.
16. And afterward the people removed Hazeroth and pitched in the wilderness of Paran.
APPENDIX 4.

Young Paul Brand 1st Observation of a Leper

Local people were always welcome at the Brand household, but when three strangers came up the mountain one day, they received a different reception. Their skin was marked with strange patches of white, their fingers were just stumps and one of them had no toes at all.

Paul watched in amazement as his father put on gloves, before he washed their feet, put some ointment on their sores and bandaged their feet. His mother brought out a basket of food for them, but kept well away from the men.

When they had gone, Paul went to pick up the basket. 'No!' - his mother's voice made him instantly draw back. He then watched in astonishment as the basket was burnt and his father scrubbed his hands with hot water and strong soap, and then changed all his clothes.

'Why are you doing all this?' asked Paul. 'Because those men are lepers,' explained his father.

A shiver ran down Paul's spine. He had heard about lepers in Bible stories, they were something bad, no one would go near them, except Jesus, who healed them.

Leprosy was the disease that everyone dreaded. People with leprosy lost the use of their hands and feet, and their faces were often disfigured. They were not able to work, and were disowned by their families. They became lonely, hopeless people, and yet there were more than 10 million of these sufferers throughout the world.
APPENDIX 5.

Obituary: Paul Wilson Brand, MD

THE LEPROSY MISSION
Janet Walmsley

A Legend has passed into history: Dr Paul Wilson Brand - 1914-2003
An Extraordinary, Gifted Orthopaedic Surgeon who Straightened Crooked Hands, unravelled
the Riddle of Leprosy; "Do the hands and feet of leprosy-affected people just fall off?
“What causes the terrible deformities of leprosy?
“Can anything be done to prevent them or restore the damage?”

Dr Brand, a modern-day Father Damian, died on Tuesday, 8th July 2003 at Swedish Hospital in
Seattle Washington, aged 89, surrounded by his wife, Dr Margaret Brand and family.

The son of missionary parents, Dr Brand spent his early years in the mountains of southwest
India. At age nine, he went to London, England for his education and later completed medical
school at London University, becoming a Fellow of the Royal College of Surgeons.
Together with his wife Margaret, whom he met at medical school, Paul Brand returned to India
in 1946 to teach surgery at the Christian Medical College and Hospital in Vellore.
Paul Brand did not set out to become a doctor. Initially he refused to follow in his father's
footsteps and study medicine, and he trained as a carpenter and builder. This skill he later used in
a remarkable way - teaching leprosy-affected people with damaged, insensitive hands how to do
carpentry and woodwork without further injuring their fingers and hands.

Very little was known about the true cause of leprosy deformities. It was generally believed that
the hands and feet of infected people simply disintegrated or rotted away as a direct result of the
disease. A senior colleague, Dr Robert Cochrane, challenged Dr. Paul Brand to use his skills as
an orthopaedic surgeon to find out why people with leprosy developed deformed hands, and to
try to find an effective treatment. Dr Brand drew on experience he had gained during WWII with
polio-paralyzed and war-injured hands. He undertook extensive research on damaged hands to
test muscle strength and sensation.

First, he pioneered the startling idea that the loss of fingers and toes in leprosy was due entirely
to infection and was thus preventable. Because leprosy attacks chiefly the nervous system,
resultant tissue abuse occurs because the patient loses the warnings of pain - not because of
inherent decay brought on by the disease. Paul Brand discovered the gift of pain, claiming that
because leprosy destroyed the sensation of pain in affected parts of the body, pain-deprived
people inadvertently injured and destroyed themselves.

Second, as a skilled and inventive hand surgeon, he pioneered tendon transfer techniques with
leprosy patients, and opened up a whole new world of disability prevention and rehabilitation for
the most vulnerable and helpless in society.
APPENDIX 5, continues

Obituary: Paul Wilson Brand, MD

In 1953 the Brands joined the staff of The Leprosy Mission, and continued to develop their research and training work at Vellore and at the nearby Schieffelin Leprosy Research and Training Centre, Karigiri, newly founded and funded jointly by The Leprosy Mission and American Leprosy Missions. In 1964 after over 17 years in India, Paul Brand was appointed as The Leprosy Mission's Director of Surgery and Rehabilitation which offered worldwide opportunities to share his life-changing skills.

Two years later they were seconded to the United States Public Health Service Hospital in Carville, Louisiana, which is the only leprosy hospital in the US and a world-famous centre for leprosy research. Here Paul was Director of the Rehabilitation Branch until his retirement in 1986 and continued to act as Medical Consultant to The Leprosy Mission.

From 1993 to 1999, Dr Brand was President of The Leprosy Mission International. In retirement Dr Brand continued to contribute to leprosy work through his advisory role to The Leprosy Mission and to the World Health Organisation. He moved to Seattle and became Clinical Professor of Orthopaedics, Emeritus at the University of Washington.

A gifted speaker and writer, Dr Brand has received many honors and awards in recognition for his outstanding achievements: he was Hunterian Professor of the Royal College of Surgeons in 1952; in 1960 he received the Albert Lasker Award for outstanding leadership and service in the field of rehabilitation; in 1961 he was honored by Queen Elizabeth II with a CBE (Commander of the British Empire) for promotion of good relations between the Republic of India and Great Britain; in 1977 the Damian-Dutton Award for outstanding contributions in prevention of disabilities due to leprosy; and the US Surgeon General's Medallion for his rehabilitation work in Carville, L.A.

Dr Brand authored 100 scientific papers and seven books, including Clinical Mechanics of the Hand, which is the premier handbook for hand surgeons, physiotherapists and other hand specialists. Co-author with Philip Yancey of three inspiring books, "Fearfully and Wonderfully Made" "In His Image", and "Pain - The Gift Nobody Wants", Paul Brand is also the subject of Dorothy Clarke Wilson's biography, "Ten Fingers for God".

Dr Paul Brand died from complications related to a subdural hematoma. He is survived by his wife Margaret, their six children, Estelle, Chris, Jean, Mary, Patricia and Pauline, and twelve grandchildren. He was a man of deep faith and passionate commitment. He was truly great, but with a natural humility that maintained to the end a hint of surprise that others should think that he had done anything outstanding. And in each person Paul Brand saw the image of God.

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APPENDIX 6

MEDICAL TREATMENT OF LEPROSY

The WORLD HEALTH ORGANIZATION recommended MDT regimen is as follows - Leprosy patients are now classified into Paucibacilliary and Multibacilliary. For both Paucibacilliary and Multibacilliary adult patients, the recommended MDT dosage of Rifampicin is 600mg. once a month. For Multibacilliary leprosy patients, an extra drug - Clofazamine - is prescribed as a supervised dose of 300mg. per month and 50 mg. daily unsupervised. Dapsone is also recommended for both paucibacilliary and multibacilliary adult patients as a dose of 100mg. daily. For children, W.H.O. recommends a monthly dose of Rifampicin at 10mg. / kg. once a month and Dapsone, daily dose of 1-2 mg. / kg.

Because of the danger of the emergence of drug-resistant leprosy bacilli, treatment must be regular and the costly Rifampicin, administered under supervision. Because of this, teams of Para-medical Workers (PMW's) personally administer MDT in the field. Patients are permitted to take home their daily doses of Dapsone and Clofazamine but Rifampicin must be administered under supervision. If, for any reason, patients are not able to report to the monthly clinic, it is the responsibility of the PMW to visit the patient in his / her home to see that the Rifampicin capsule is actually consumed.
APPENDIX 7

DETAILED HISTORY OF MDT APPROACHES

To overcome the serious threat posed by the widespread emergence of dapsone resistance, and to increase the therapeutic effect in chemotherapy of leprosy, a World Health Organization (WHO) Study Group in 1981 recommended multidrug therapy (MDT) for the treatment of leprosy. It was recommended that, for the purpose of treating different categories of patients with various bacterial loads, leprosy be classified as paucibacillary (PB) and multibacillary (MB), and that two drugs, monthly rifampicin (RMP) and daily dapsone (DDS), be prescribed for the treatment of PB leprosy, and three drugs—daily DDS and clofazimine (CLO) together with monthly RMP plus a supplemental higher dose of CLO—for MB leprosy. The duration of MDT for PB leprosy is 6 months; whereas for MB leprosy, it was recommended that MDT should be given at least 2 years and preferably be continued up to skin-smear negativity. Because of the promising results of 24-month treatment, the WHO Study Group recommended, at its second meeting in 1994, that all MB leprosy should be treated for 24 months. The MDT regimens have proved to be highly effective and well tolerated by the patients. At the beginning of 1997, more than 84 million leprosy patients had been cured by MDT. However, from the operational point of view, the duration of MDT is still too long, especially for MB leprosy. The long duration of treatment has become one of the major obstacles in implementing MDT, particularly in areas where the health infrastructure is poor or the accessibility is difficult. It would facilitate the implementation of MDT among all patients who need treatment if the duration of MDT could be further shortened without significantly compromising its efficacy.

To avoid relapse caused by spontaneously occurring RMP-resistant mutants and to minimize the relapse due to drug-susceptibility organisms after stopping MDT, the appropriate duration of MDT for MB leprosy is the time required to reduce the size of viable bacterial population to such an extent that RMP-resistant mutants are completely eliminated and the great majority of drug-susceptible organisms are killed. To date, due to technical constraints, we are unable to determine directly, with any laboratory tool, whether or not the RMP-resistant mutants are still present in the hosts, or whether the drug-susceptible organisms are reduced to a negligible level. However, the following information may be useful to define the appropriate duration of MDT for MB leprosy.

First of all, the definition of MB leprosy has become much broader since 1981, when the Study Group designed the MDT regimen. Originally, MB leprosy referred to those patients who had a bacterial index (UI) of ≥ 2 at any site in the initial skin smears. A few years later, the WHO Expert Committee on Leprosy at its 6th Meeting modified the definition that all skin smear positive cases should be classified as MB leprosy; and the Second WHO Study Group further recommended that, when the classification is in doubt, the patients should be created as having MB leprosy. Then, because of the lack of dependable skin-smear facilities in most leprosy programs, the WHO Expert Committee on Leprosy at its 7th Meeting proposed that patients could be classified on clinical grounds only, and that MB leprosy should refer to those having more than five skin lesions. These modifications have resulted in the classification of many cases that would otherwise be PB leprosy as MB leprosy, and the proportion of MB leprosy among
newly detected cases has increased from 20.8% in 1985 to 30.9% in 1996. A more important finding is that, unlike in the early 1980s when all newly detected MB cases were skin smear positive, the proportion of smear positive cases among newly detected MB leprosy cases in 1996 was less than half. Among 142,844 newly detected MBN cases from the 16 major leprosy endemic countries, it was estimated that 69,449 (48.6%) were skin smear positive, and only 24,216 (17.0%), or one-sixth, of MB cases have a BI of ≥3.7 Because the bacterial loads of the majority of MB patients currently classified are significantly smaller than those in the past, the overall requirements of chemotherapy for MB leprosy may also be less.

Secondly, the results from both routine control programmes\textsuperscript{8} and from research projects\textsuperscript{9} have demonstrated that the relapse rates after MDT were very low, about 0.2% annually, among MB leprosy cases. Similar results have been obtained after 2-year fixed duration MDT.\textsuperscript{10–14} The low relapse rates indicate that there is enough room for further shortening the duration of MDT to less than 24 months. Although some reports suggested that relapse rates after MDT could be significantly higher among MB patients with a high initial BI, i.e. the average BI ≥ 4.0,\textsuperscript{15,16} because such patients have become relatively scarce in the field,\textsuperscript{7} the total number of relapses by them contributed to a leprosy control programme will be small. The programmes should accept the few relapses that may occur from patients with a high initial BI and treat those patients who do relapse with a further course of MDT.

Thirdly, the major role of the DDS-CLO component of the MDT regimen for MB leprosy is to ensure the elimination of the spontaneously occurring RMP-resistant mutants. estimated to be no greater than $10^{3}$ organisms in an untreated patient with lepromatous leprosy,\textsuperscript{17} before stopping chemotherapy. The results from both nude mouse experiments\textsuperscript{18} and a clinical trial\textsuperscript{19} have demonstrated that the bactericidal effect of the DDS-CLO component was significantly greater than expected; 3 months of daily treatment with DDS-CLO component alone killed more than 99.9999% of viable Mycobacterium leprae,\textsuperscript{18} suggesting that all the spontaneously occurring RMP-resistant mutants are likely to be eliminated by 3–6 months of treatment with the DDS-CLO component in the MDT regimen.

Fourthly, in a multicentre, double-blind trial organized by the Steering Committee on Chemotherapy of Mycobacterial Diseases (THEMYC) of the UNDP/World Bank/WHO Special Programme for Research and Training in Tropical Diseases, MB patients with initial BI ≥ 2 were randomized into four groups of about 500 patients each, and two of the four groups were treated, respectively, with 24-month or 12-month MDT. After 4–6 years of follow-up from intake, or 3–5 years after stopping treatment with the 12-month regimen, not a single relapse has been detected among the two groups, which suggests that the 12-month MDT is as effective as the standard 24-month MDT regimen (THEMYC Steering Committee, unpublished data). The efficacy of various durations of MDT has also been compared in a clinical trial in Malawi, in which 305 MB cases were randomly allocated into two groups and treated, respectively, with 18 or 30 months of MDT.\textsuperscript{20} After stopping treatment, the mean duration of follow-up was 3 years, with a maximum of 6 years. In both groups, the BI continued to fall, and fell to 0 by 60 months
APPENDIX 7 continues

DETAILED HISTORY OF MDT APPROACHES^44

of follow-up. No relapse was observed in either group and the percentage of patients who developed new disabilities was similar. It was concluded that 18-month MDT may be sufficient for the treatment of MB leprosy.

Finally, information on the clinical and bacteriological progress of defaulted MB cases may shed some light on the efficacy of MDT with duration shorter than the standard one. In one study,^21 41 defaulted MB cases were retrieved. They had been treated with MDT for a mean duration of 7 months (range 3–13 months), and had not taken treatment after defaulting. By the time the patients were retrieved, from less than 1 year to more than 5 years after drop-out, all 41 patients showed clinical improvement, and 29 (71%) became smear negative, while the BI was stationary in five (12%) cases. In another series of patients,^7 who were skin smear positive before defaulting, 139 and 95 of them had been treated, respectively, with <12 months and 13–23 months of MDT before defaulting. By the time the patients were retrieved, after a mean duration of drop-out for 7.6 and 7.5 years, respectively, only 11 (7.9%) patients from the former and six (6.3%) patients from the latter group were still smear positive. Not only were the positive rates very similar between the two groups, but neither differed significantly from those (33%) of 761 patients who had completed 24 months of MDT and were examined 4 years later. Although one has to be cautious in interpreting the information from the retrospective analyses, because the records are often incomplete, the sample size is relatively small and the pretreatment characteristics of the patients between the groups may not be comparable, they do suggest that treatment with less than 12 months of MDT exhibited promising therapeutic effects among the majority of MB patients.

On the basis of all the available information, the WHO Expert Committee on Leprosy concluded, at its latest meeting in 1997, that it is possible that the duration of the MDT regimen for MB leprosy could be further shortened to 12 months.^5 This conclusion has been well-accepted by almost all the leprosy control programmes of the major endemic countries and is being implemented. Of course, during the transitional period from 24-month MDT to 12-month, a series of operational issues should be addressed, such as providing guidelines for the transition, revising national manuals, introducing a new reporting system, and improving the detection and treatment of leprosy reactions after completion of treatment. However, compared with the earlier days when MDT was introduced, in most countries now the leprosy control programme managers and their field staffs are more experienced, and they are able to handle these operational issues without too much difficulty.

B. Ji, MD, Faculté de Médecine Pitié-Salpêtrière, 91 Boulevard de l’Hôpital, 75634 Paris Cedex 13, France
APPENDIX 7 continues

DETAILED HISTORY OF MDT APPROACHES

References

APPENDIX 8

LEPROSY ELIMINATION DOES NOT EQUAL ERADICATION

Leprosy is an infectious disease but it has many features in common with neurodegenerative disorders. It results in a chronic neurological illness, which is progressive unless treated; frequently produces long term disability; and is associated with high levels of stigma. As it has a known infective agent, Mycobacterium leprae, there is the possibility of disease control. Multidrug treatment with the antibiotic combination rifampicin, dapsone, and clofazimine is highly effective in curing infection, with relapse rates of 1%. It was hoped that having effective antibiotics would permit disease control and thus the concept of leprosy elimination developed. "Leprosy elimination by the year 2000" was first proposed in 1986 and at the 44th World Health Assembly in 1991 modified by the addendum "as a public health problem," defined as less than one case per 10,000 population. The leprosy elimination campaign has had some notable successes but also illustrates the epidemiological, medical, and political problems of the elimination concept.

Summary points Leprosy is a leading cause of neurological disability The World Health Organization's leprosy elimination campaign has treated 11 million patients, but case numbers are still rising in the major countries where leprosy is endemic New methods for diagnosis and treatment proposed by the WHO risk missing disease and undertreating patients, and an opportunity for implementing evidence based policies may be missed

Controlling and treating leprosy

Leprosy is a complex mycobacterial disease whose manifestations and complications are determined by the immune response. Many patients experience immune mediated nerve damage, which may occur before, during, or after treatment. Recent field based cohort studies have shown that at diagnosis many patients already have established nerve damage; rates vary from 20% in Bangladesh to 56% in Ethiopia, and these patients have a worse prognosis for disability. Up to 30% of multibacillary patients have acute inflammatory episodes (reactions) affecting skin and nerves. Prednisolone is used to suppress reactions and ameliorates acute nerve damage in about 60% of patients. Anesthesia and paresis in the hands and feet put them at risk of secondary damage from trauma and infection, which cause the highly visible deformities of leprosy. The purpose of controlling leprosy is to reduce the rate and severity of disability. The key to effective management of leprosy is early diagnosis and treatment and early recognition and management of nerve damage, combined with effective health education.

WHO clinical classification for field programmes. Paucibacillary single lesion leprosy (one skin lesion) · Paucibacillary (two to five skin lesions) · Multibacillary (more than five skin lesions) Neurological assessment and slit skin smears do not contribute to this classification.
APPENDIX 8 continues

LEPROSY ELIMINATION \textit{DOES NOT EQUAL} ERADICATION

What has the elimination campaign achieved? People and governments were mobilized, leprosy programs were revitalized, and drug treatment for leprosy was provided free of cost by the Sasakawa Foundation through the World Health Organization. Imaginative programs were devised, such as monthly drug delivery circuits by paramedical workers to supervise taking the monthly components of multidrug therapy. Morale among patients and workers improved. Eleven million patients have been given multidrug therapy. The number of registered patients fell from 5 million in 1985 to 0.7 million in 2001. But this fall was almost entirely attributable to a change of case definition that includes patients only during the course of multidrug therapy that is, those with active infection.\textsuperscript{6} Patients with ongoing complications or disabilities due to the disease are excluded.

In 2001 WHO claimed that leprosy had been eliminated "at a global level," even though 719,330 new patients were registered in 2000.\textsuperscript{7} In the 27 top countries where leprosy is endemic, the incidence did not fall between 1985 and 1999, and in the six countries that account for 88% of new cases the numbers and incidence of new cases are rising (figs 3 and 4).\textsuperscript{9} Children comprise 15% of cases, indicating that active transmission continues. WHO has now rescheduled elimination for 2005. Integration of previous leprosy-only programs into primary health care is the preferred model. Leprosy is not an easy disease to diagnose, and patients seen at peripheral clinics will go undiagnosed, thus apparently reducing the incidence of the disease further.

Policy changes should be evidence based

The enthusiasm of the WHO for simplifying leprosy management threatens the achievements of the elimination campaign. Numerous policy changes have emanated from the WHO for direct implementation in the field without prior research. Skin smears, essential for identifying patients with high bacterial loads, have been discontinued and the duration of multidrug therapy for multibacillary patients has been reduced from 24 months to 12 months despite evidence that patients with high bacterial loads are at greater risk of relapse.\textsuperscript{10}

Policies for leprosy control can be evidence based, as has been shown by an expert group convened by the International Leprosy Association this year. The group produced evidence based graded recommendations on issues relating to leprosy control, diagnosis and classification, chemotherapy, nerve damage and rehabilitation, and sustainability of leprosy services (www.lepra.org.uk/).\textsuperscript{13} Simplifying diagnosis has been considered by both the WHO and the evidence based group; the WHO document states that in 70% of patients, diagnosis can be made by a single sign: an anesthetic skin patch. The evidence based group found that the other 30% are multibacillary patients, who are more likely to be infectious and to develop nerve damage.
APPENDIX 8 continues

LEPROSY ELIMINATION \textit{DOES NOT EQUAL} ERADICATION

The elimination of leprosy will be a virtual phenomenon elimination of registered cases through very short treatment regimens without reducing the number of new cases. The concept of elimination at a prevalence of one case per 10 000 population is a difficult concept to understand, and many people confuse it with eradication. There is no evidence that reaching this predefined prevalence will reduce transmission, incidence, or the annual number of new cases. Who needs this prize, and must it be delivered at all costs? The elimination campaign has shown how difficult it will be to eliminate leprosy in countries where it is highly endemic. The biology of the organism and the disease mitigate against easy control of transmission. Lepromatous patients are highly infectious through their nasal secretions; the organism can survive many months outside a human host; up to 5% of the population in leprosy endemic areas are nasal carriers of \textit{M leprae} DNA.\textsuperscript{14} Lepromatous disease has a mean clinical incubation time of 10 years.\textsuperscript{15}

If the WHO believes its own rhetoric about eliminating leprosy, then governments of countries where leprosy is endemic may believe it too and disband their control programs and disperse their skilled staff. But they may be left with many unanswered questions. Who will provide drug treatment after 2005? \textbf{What plans are being made for the long term care of patients with nerve damage, who will continue to present for many years to come?} In the 1960s tuberculosis and malaria were pronounced defeated; now we face global emergencies in control and management for both diseases. It would be tragic to see this cycle repeated with leprosy.
APPENDIX 8 continues

LEPROSY ELIMINATION \textit{DOES NOT EQUAL} ERADICATION

REFERENCES:

APPENDIX 9

LEPROSY in ECUADOR: NEUROSENSORY TESTING

Distribution of Peripheral Nerves Evaluated with Neurosensory Testing

<table>
<thead>
<tr>
<th>Peripheral Nerve</th>
<th>Number of Nerves Tested</th>
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<tr>
<td>Ulnar</td>
<td>40</td>
</tr>
<tr>
<td>Radial Sensory</td>
<td>2</td>
</tr>
<tr>
<td>Peroneal</td>
<td>30</td>
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<tr>
<td>Tibial</td>
<td>18</td>
</tr>
<tr>
<td>Sural</td>
<td>1</td>
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<tr>
<td><strong>Total</strong></td>
<td><strong>120</strong></td>
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Documentation and Staging of Peripheral Nerve Dysfunction with the Pressure-Specified Sensory Device™

Grading of Degree of Sensory Nerve Compression

<table>
<thead>
<tr>
<th>Peripheral Nerve</th>
<th>(Mild-Moderate)</th>
<th>(Severe)</th>
<th>(Anesthetic)</th>
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<tbody>
<tr>
<td>Median</td>
<td>41%</td>
<td>24%</td>
<td>35%</td>
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<td>Ulnar</td>
<td>35%</td>
<td>37%</td>
<td>28%</td>
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<tr>
<td>Peroneal</td>
<td>10%</td>
<td>13%</td>
<td>77%</td>
</tr>
<tr>
<td>Tibial</td>
<td>11%</td>
<td>16%</td>
<td>73%</td>
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## APPENDIX 10

**LEPROSY in ECUADOR: POST-OP REPORTING FORM**

<table>
<thead>
<tr>
<th>Name:</th>
<th>Grace Zambrano Cabrera</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Intervention:</strong></td>
<td>Left Ulnar, Radial, Median</td>
</tr>
<tr>
<td></td>
<td>Right common Peroneal, deep Peroneal, posterior Tibial</td>
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</table>

<table>
<thead>
<tr>
<th><strong>Evolution:</strong></th>
<th></th>
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</thead>
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<tr>
<td>Oct, 4/04</td>
<td>L-Hand: Suture material is taken off from her hand, and it could be seen an excellent scar. Patient said sensibility is better than before</td>
</tr>
<tr>
<td>Oct, 11/04</td>
<td>R-Foot: The suture material is taken off from the foot. The incision is becoming healing, no pain. Patient say there is no changes with sensibility or movements</td>
</tr>
<tr>
<td>Oct, 20/04</td>
<td>L-Hand: There are not any changes with sensibility and movements. R-Foot: common peroneal incision is healing; deep peroneal and posterior tibial incisions are with a rash and red skin but no infection signs. Patient says there's no pain and there are no sensibility and movements changes. Rash is on her arms, neck and legs too</td>
</tr>
<tr>
<td>Nov, 17/04</td>
<td>L-Hand: Has recovered same sensation + mobility. Hand is much better. R-Foot: Have better sensation on both top and bottom of foot</td>
</tr>
<tr>
<td>Dec, 15/04</td>
<td>L-Hand: she can feel better now. Also she can do a lot of things she couldn't before surgery, like lift a bucket normally. R-Foot: Has better sensibility on both top and bottom of foot.</td>
</tr>
<tr>
<td>Jan, 18/05</td>
<td>L-Hand: now she can feel the presence of close hot objects and whether something hurt her, she can feel pain. Sensitivity of index and small fingers is better compared to another hand. She can do many things she couldn't before, like brush her hair or hold a washbowl.</td>
</tr>
</tbody>
</table>

Before surgery she held the washbowl like this picture

Now she can hold it like this picture

R-Foot: before surgery she described her pain as 10 on a 0-10 scale; now it is 8. Sensitivity on plantar surface, the top or the foot and the lower leg is as well as the other foot. Does not have any difference in sensitivity. She can move her toes and she has good strength in big toe.
## APPENDIX 10 continued

**LEPROSY in ECUADOR: POST-OP REPORTING FORM**

<table>
<thead>
<tr>
<th>Name:</th>
<th>Pastor Ávila Vera</th>
<th>Dr. Dellon</th>
<th>Dr. Wilton</th>
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<tbody>
<tr>
<td><strong>Intervention:</strong></td>
<td>Left Ulnar, Radial, Median</td>
<td>Right common Peroneal, Left common Peroneal</td>
<td></td>
</tr>
<tr>
<td><strong>Evolution:</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Oct, 4/04</td>
<td>L-Hand: Suture material is taken off from the hand, and it could be seen an excellent scar.</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Oct, 11/04</td>
<td>RL-Feet: The suture material is taken off from right and left foot. The incisions are excellent. Patient says there is some difficult to walk, he could walk better before the surgery. He has feet ached, but it is not to strong.</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Oct, 20/04</td>
<td>L-Hand: Excellent incisions scar, there is not any changes with sensibility and movements. There is not pain also. RL-Feet: excellent incisions scar. Patient says he has some problems to walk: &quot;instability&quot;. Common peroneal incision is healing; deep peroneal and posterior tibial incisions are very well. He can feel better on the top of his foot.</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Nov, 17/04</td>
<td>R-Foot: Has limited dorsal flexibility and sensation in right foot on bottom can not spread toes. But the right knee reflex is good. L-Foot: Has dorsal flexibility and can spread toes. Has poor knee reflex. Has lees sensation. The bottom of the foot is “asleep”</td>
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<td>Dic, 15/04</td>
<td>L-Hand: there are not changes about sensibility or movements. RL-Feet: he still has problems to walk, ha needs a walking stick and he feels instability. He starts a rehabilitee therapy.</td>
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<tr>
<td>Jan, 18/05</td>
<td>L-Hand: sensitivity worsened after the surgery. Now has more sensitivity in the other hand. No changes in strength; does no have strength to lift objects the same as before surgery. If he tries to hold something, it falls from his hands. Feet: Pinch Open and extended Closed Open and together Straight up</td>
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<tr>
<td>R-Foot: has planter reflex. There is no strength in the big toe and little sensitivty. It was better before the surgery. L-Foot: has no planter reflex, cannot feel anything. On January 9th, he suffered a convulsion, after which he had monopelgia in the right leg. Causes unknown, awaiting results from CAT scan but the family has not be able to do anything (due to lack of funds)</td>
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<tr>
<td>Jan, 27/05</td>
<td>There were find two tumours in his brain and another one in his lung.</td>
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<tr>
<td>Feb, 6/05</td>
<td>Mr Ávila died at 6 PM</td>
<td></td>
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</tbody>
</table>
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