From an Elegy on Leprosy, Bergen, 1820, to Elimination of Leprosy in India by Multidrug Blister Calender Packs 1986-2003

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Accompaniment on Violin:
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UNIVERSITY OF COPENHAGEN

This lecture is dedicated to late *Prof. V. Møller Christensen*, who summarised **sufferings** of lepers: [they] "were housed ⋯ and cared for. No return was possible. Just as the River Jordan runs into the Dead Sea, so that all wreckage carried by the river will come to rest in the Dead Sea, so it has been with the lepers – the outcasts- who were admitted to a **St. Jørgen's hospital.** Rich or poor, squire or beggar, when they first came here, Journey's end sooner or later was the leprosy graveyard"

…aeological, historical, palaeopathological and clinical approaches

Figure 13: 'I remember marvelling at the unconcerned way in which Vilhelm walked through the streets carrying skulls in a string bag, oblivious of the sidelong glances of passers-by' (Jopling in (Møller-Christensen, 1978: 8-9).

Lepr Rev (1989) **60**, 157

Obituary

VILHELM MØLLER-CHRISTENSEN MD
1903–1988

Vilhelm Møller-Christensen died at the age of 85 in his home town of Roskilde, Denmark, on 15 November 1988. In 1941, as a general practitioner with a special interest in medical history and paleopathology, he began a series of excavations in the burial ground of a large medieval Augustinian Abbey in Aebelholt, North Sealand. Three years later he unearthed a skeleton with puzzling bone changes which he suspected might be due to leprosy, even though it was not customary in the Middle Ages to bury leprosy sufferers in monastic cemeteries. As these puzzling bone changes could not be explained by contemporary leprologists and paleopathologists, he decided to gain information by finding the graveyard of one of the 30 or more St Jørgen's (St George's) hospitals which were thought to have housed Danish leprosy sufferers in the Middle Ages. Hearing that human bones had been accidentally unearthed near Naestved, South Sealand, in the region where a St Jørgen's hospital had existed, he began a systematic search for the site. Travelling from farm to farm making inquiries, he reached a dairy farm where the owner admitted to having found human bones when digging a drain in the farmyard, so in 1948 he began exhumations at this site, aided by Naestved Museum and the National Museum of Copenhagen, and funded by the Carlsberg Foundation. Further work revealed that he had found a St Jørgen's hospital, which had existed between 1250 and 1550, thus establishing that leprosy was a health problem in north-west Europe in the Middle Ages. The last exhumations were carried out in the summer of 1968, enabling him to complete his meticulous studies of skeletal material from about 650 persons, bringing to light some previously unknown changes of leprosy, particularly those in the rhinomaxillary region of the skull which he named *facies leprosa*. He recorded his observations in a number of papers and books, the last being *Leprosy Changes of the Skull* (1978).

During these years he studied clinical leprosy in Malaya and Thailand, and visited leprologists and paleopathologists in various capitals of Europe, accompanied by his inseparable travelling companions in the form of a selection of bones and skulls from Naestved. When I spent a week with him in 1963, looking for signs of *facies leprosa* in the skulls of the Catacombs in Paris, I recall marvelling at the unconcerned way in which he walked through the streets carrying skulls in a string bag, oblivious of the sidelong glances of passers-by!

In 1964 Vilhelm Møller-Christensen was appointed Professor of Medical History at the University of Copenhagen, later becoming Professor Emeritus, and in the same year he was appointed Director of the University Medical History Institute and Museum. In the latter capacity he spent much time and care in establishing within the Museum a leprosy section containing the best osseous material from Naestved. He was President of the Danish Society of the History of Medicine from 1964 to 1974, and Director of the World Health Organization Institute for the History of Leprology in 1973. Honours conferred on him included that of Knight of the Order of Danneborg (1954), and Commander of the Papal Order of St Silvester (1973).

Vilhelm Møller-Christensen has won a well-deserved place in the annals of medical history, leprology, and paleopathology.

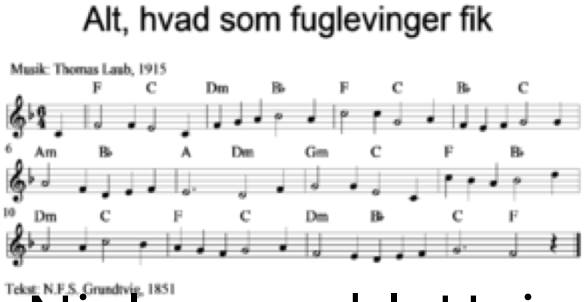
W H JOPLING

Leprosy (Hansen's (1873) disease), European region

- V Møller-Christensen: Earliest evidence probably in 6.th century A.D. (Egypt, France, Britain)
- Maximum in Christianity 13.th century, 19,000 leprosaria, (possibly unnecessary isolation of tuberculoid leprosy – which made up 80% in most parts of the World)
- Decline from 14.th century, leprosaria re-used as quarantaine stations for plague
- Cause of decline: Isolation or rise of Tuberculosis?

En Klagesang af Peder Olsen Feidie
A Mourning Song, verse 12,13,14

- **Isolation of lepers** was considered ‘best practice’ in leprosy control till modern multidrug therapy was launched in the early 1980s. Peder Olsen Feidie, patient **at Sct. George’s Leprosarium** (Skt. Jørgens Hospital), **Bergen**, Norway, was isolated for life as a young man and expressed what that implicated in a Mourning Song (“**En Klagesang**”).
- Melody:



- Violin: Casper Nielsen, cobl, University of Copenhagen
- Chorus: **all!**

English ‘translation’ by I.B., Original by P.O.F.verse 11

- **11. I walk the floor by night so ‘lone**
- **When patients all to bed have gone,**
- **can hardly hear their mourning.**
- **The first repeats: poor me, poor me!**
- **The second adds: Oh Lord, let it be!**
- **How oft’ go back to my couch,**
- **Before Your grace may reach out.**

- **11. Jeg gaar paa Gulvet af og til,**
- **naar alting er i Huset still',**
- **da høres Sørgetoner.**
- **Den ene raaber Ak og Vee,**
- **Den anden klager sig dermed**
- **at han maa gaae til Senge.**
- **Ak, Herre Gud! hvorlænge.**

English translation by I.B., Original by P.O.F.verse 12

- **12. The first disfigured: sore on sore.**
- **the Second walks on toes no more.**
- **the Third is mute – only sighing,**
- **the Fourth: day-light for always is banned,**
- **the Fifth for ever lost nose and hand.**
- **Five senses, no more to offer:**
- **Behold! And recon' what we suffer!**

- **12. Den ene haver Saar i Saar,**
- **den Anden han paa Krykker gaaer,**
- **den Tredie kan ei tale,**
- **den Fjerde kan ei Dagen see,**
- **den Femte har ei Hænderne,**
- **Saa kan Enhver vel vide,**
- **Hva Ondt vi her maa lide.**

English translation by I.B., Original by P.O.F. verse13

- **13. Inside Sct. Georges's Hos-pital**
- **by hundreds, lepers waiting shall,**
- **for leaving and re-lieving,**
- **this Earthen Valley of dis-grace,**
- **and for the Farther and His grace,**
- **their souls shall stand exalted,**
- **disfiguerings, sufferings halted!**

- **13. I Sancte Jørgens Hospital,**
- **ja over hundred er i Tal,**
- **som venter paa at løses.**
- **O Helligaand vær Styremand,**
- **og føer os saa til Himlens Land.**
- **Did Sjelene vil gange,**
- **der løses alle fangne.**

Pathological pattern of leprosy

- High CMI -> Low no. of bacilli, TT
  paucibacillary or
  tuberculoid,few skin
  elements, well-demarcated,
  early nerve-involvement
- Low CMI -> High no. of bacilli, LL
  multibacillary or **lepromatous**,
  many skin lesions, not well demarcated,
  late nerve involvement
- **Borderline** – in between, may shift up or down = danger of reactions!

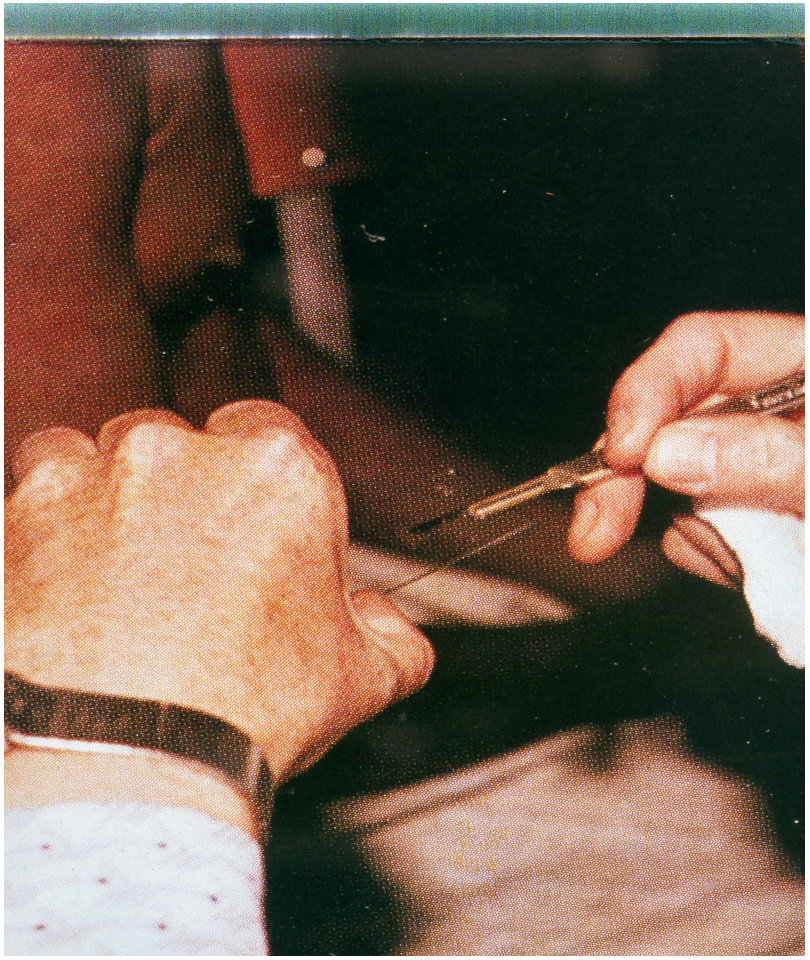
Indeterminate = early, single discrete depigmented spot

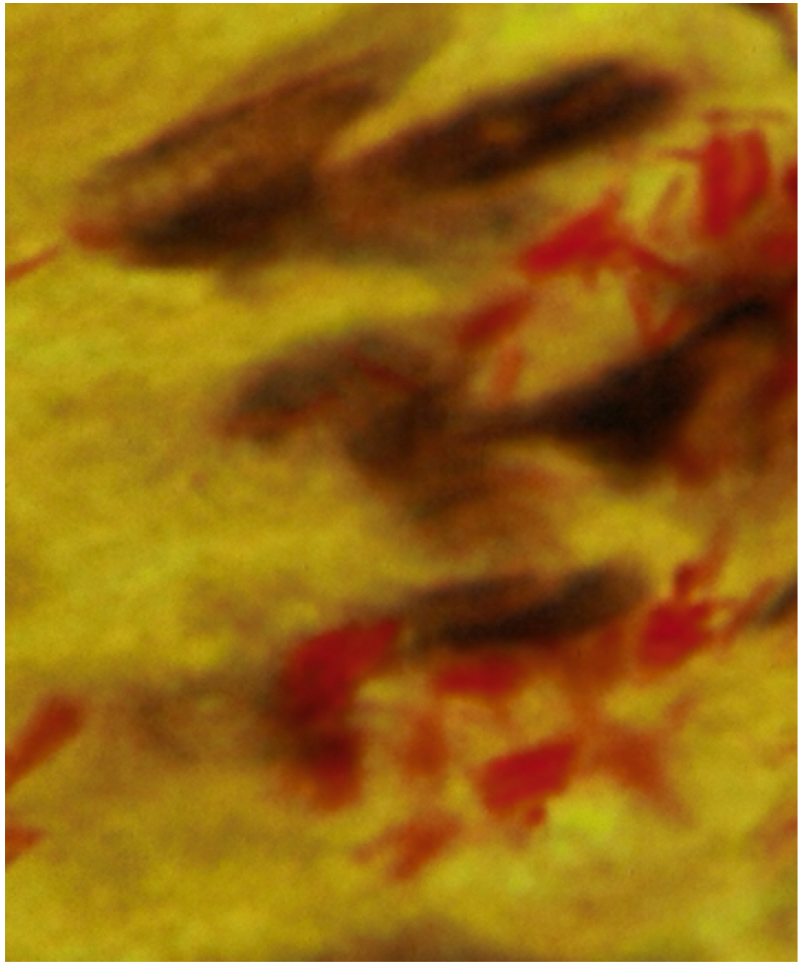
Clue to diagnosis of leprosy

- Origin of patient – f.ex. India, Indonesia, Brasil, SSAfrica
- No sensitivity,
- No sweat on spot
- Palpable regional nerves, palsies
- Late stages:

  Lion face, Lack of eye-brows,
  Gynecomastia in males
  Absorption of digits. NB! Nails remain
  Absorption of spina nasalis, Loss of upper Incisors (teeth) Remember eyes!

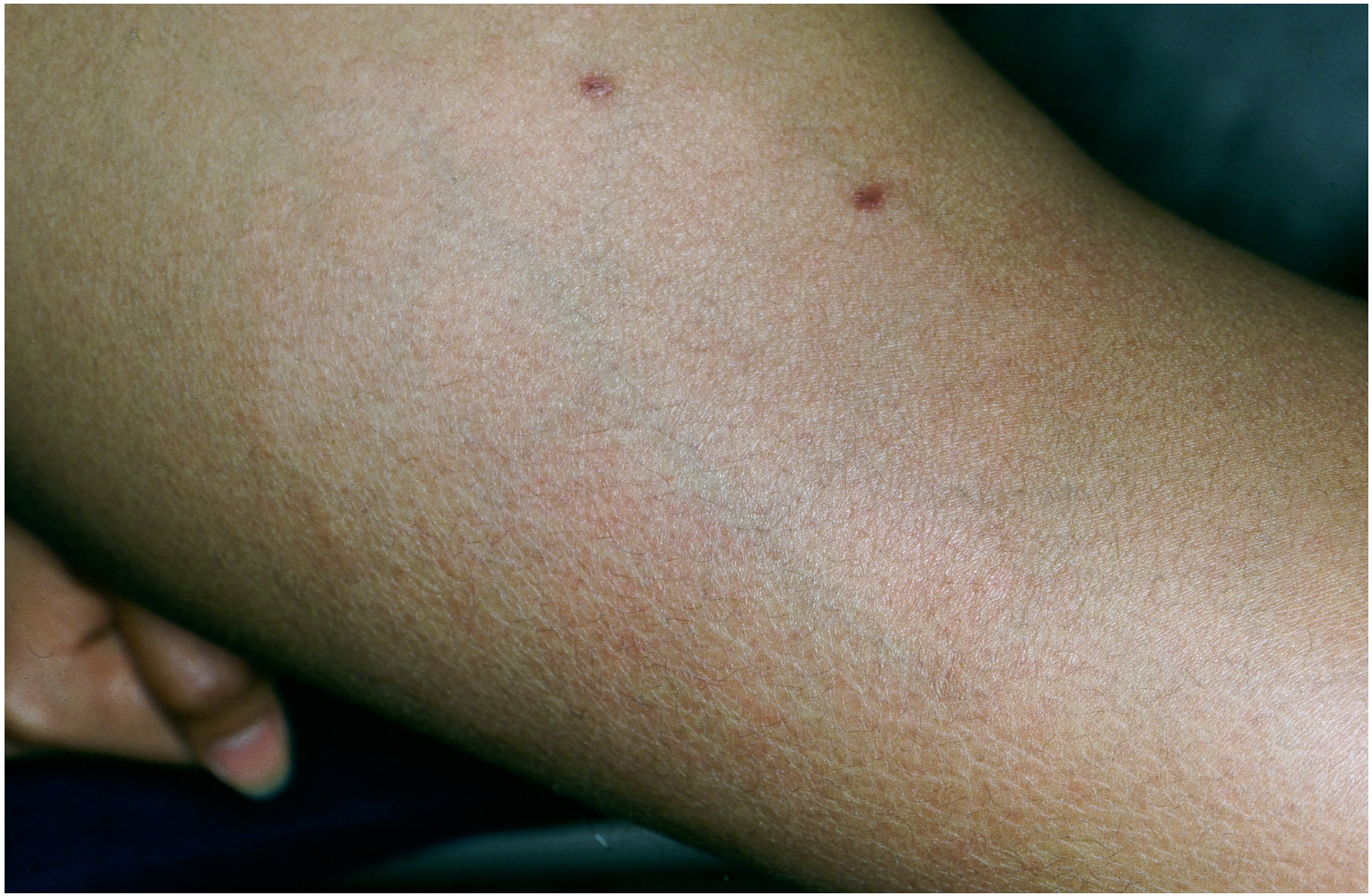
Diagnosis: skin smear or biopsy from border of lesion or cool parts of body (earlobes), stain and microscopy





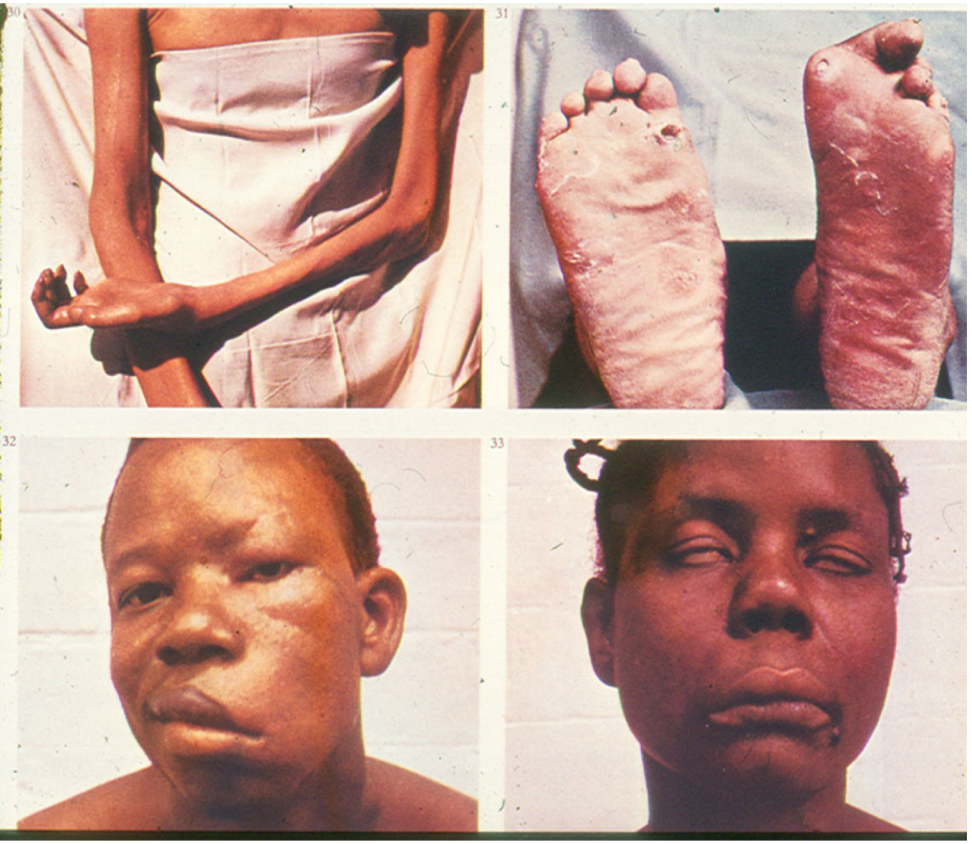
Sometimes very descrete depigmentation in early cases – but lack of sensitivity prompted diagnosis.

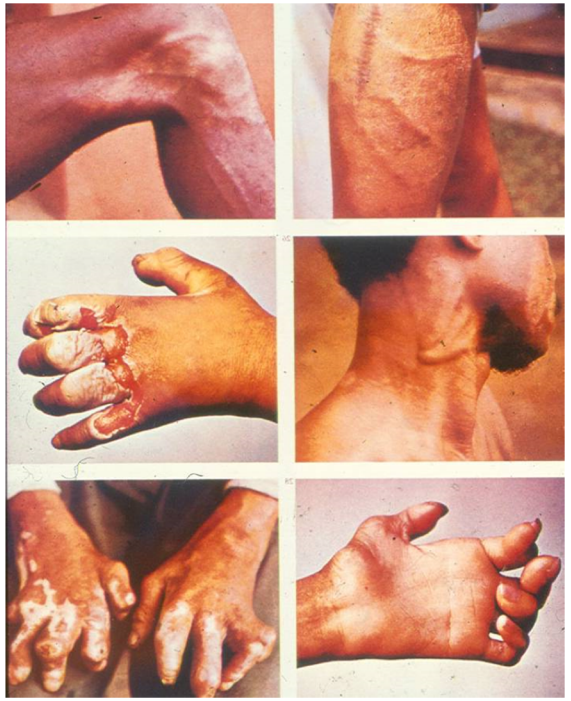
Two darker spots are sequels after biopsies



Philipino au-pair girl I diagnosed some years ago

Too late diagnosis with severe nerve damage, blindness, claw-hand, absorption of digits, and ulcers.





After decades of ineffective treatments, most recently Dapsone monotherapy, WHO, 1982 introduced **modern multidrug chemotherapy** (MDT):

Paucibacillary: 6 mo. Dapsone daily + rifampicin x 1 monthly;

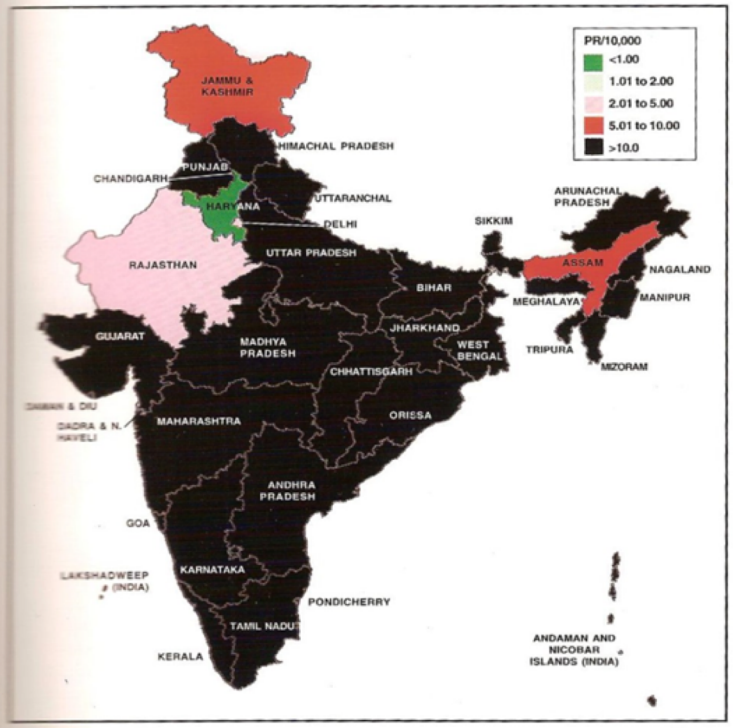
Multibacillary: 24 mo. DDS daily + Rif x 1 monthly + clofazimine daily and monthly

- In 1997, the 7th WHO Expert Committee considered that duration of treatment of MB leprosy could be reduced to 12 months without compromising the efficacy of the MDT regimen

Bleak leprosy situation in India, by 1981:
Most states 'black', with prevalence > 100 pr. 10.000.

By 1986, not much better;
World-wide, MDT not accessed
by 70% of leprosy patients

Figure 1
Map of India showing state-wise leprosy prevalence in 1981



"India pledges to whipe out leprosy with the new drugs"

Leprosy Elimination in India

The DANLEP Experience

1986-2003

Chitra Sundaram
Gita Narayanan

NLEP slogan from the 1980s

भारत ने ठाना कुष्ठ मिटाना
नई दवाएं कुष्ठ मिटाएं

இந்தியாவின் முனைப்பு
தொழுநோயின் ஒழிப்பு !
கூட்டு மருந்து
தொழுநோயை ஒழிக்கும்!

ଭାରତରେ ରହିବୁ ଆମେ
କୁଷ୍ଠ ଯିବ ଦୂରେଇ,
ନୂଆ ଔଷଧ ଖାଇବୁ ଆମେ,
କୁଷ୍ଠ ଦେବୁ ହଟାଇ

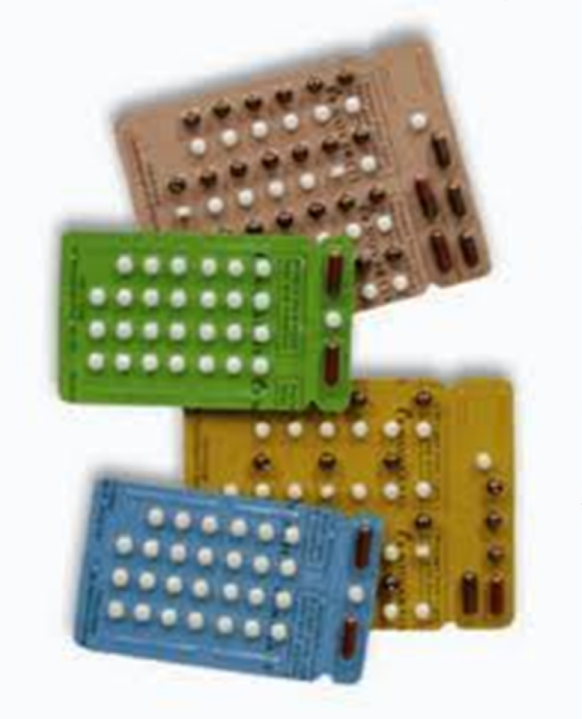
India pledges to wipe out leprosy with the new drugs

Indien står fast på at udrydde spedalskhed med den ny medicin

Sources: **The DANLEP Experience 1986-2003.** Chitra Sundaram , Gita Narayanan & **Blister calendar packs for the implementation of multiple drug therapy in DANIDA-assisted leprosy control projects in India. Danish International Development Agency.** Georgiev GD, Kielstrup RW. Lepr Rev. 1987 Sep;58(3):249-55.

- In 1st DANLEP/NLEP program year, multidrug therapy (MDT) in form of loose drugs.
- To overcome compliance problems and confusion, blister calender packs proposed by Danida.
- MDT Blister packages designed & manufactured by Pharmanova, Copenhagen.
- Blister packages became key in eradication programme, supported by World Bank, and DANLEP.
- In 1997, WHO took over in India, and Scanpharm, DK.
- In 2000, Novartis provided worldwide MDT blister packages via WHO, free of charge.

Kielstrup, personal communication 1988



improving patient compliance

having just completed a hasty review of current literature on patient compliance, i've come across some statistical data and general observations which will probably interest you:-

table 5:
important strategies for improving patient compliance
(results of studies including control groups)

	improvement in patient compliance
1. calendar packs	+ 34 percent
2. verbal patient counselling and education	+ 22 percent
3. patient information leaflets	+ 22 percent
4. house visits	+ 15 percent
5. reminding patient in writing of forthcoming appointment	+ 10 percent
6. high expectation of efficacy as perceived by the patient (product colour, pack presentation and other psychological factors may influence patient perception of drug efficacy)	positive

Lepr Rev. 1989 Jun;60(2):135-8.

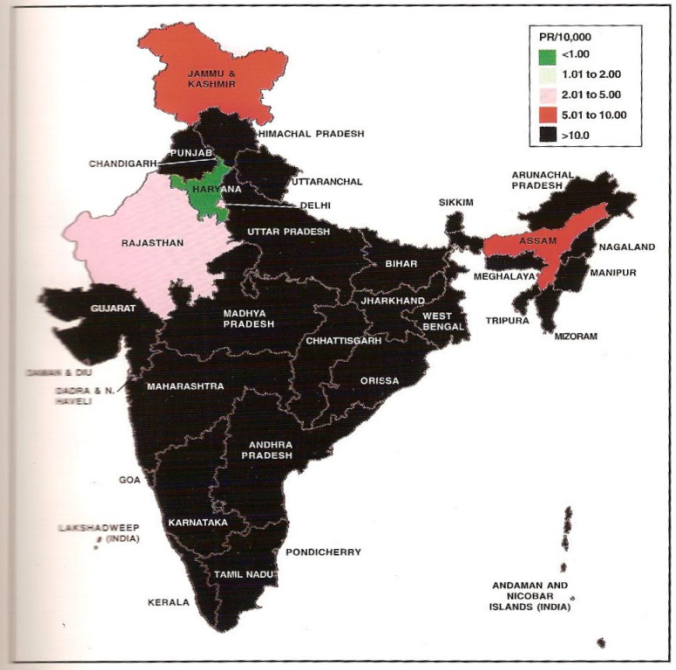
Delivery of MDT through blister calendar packs in leprosy eradication programmes--a multicentre field study (phase I). Multicentre Study Group.

Revankar CR, Sorensen BH, Kielstrup RW.

- To overcome operational problems and improve patient compliance in leprosy programmes, DANIDA introduced blister calendar packs (BCP) to deliver MDT in four districts in India.
- A questionnaire study of 1470 patients from these districts showed that more than 90% accepted BCP and found them to be very convenient for domiciliary treatment.
- A similar study of 127 treatment providers indicated that delivery of MDT through BCP was found convenient to overcome logistic problems.

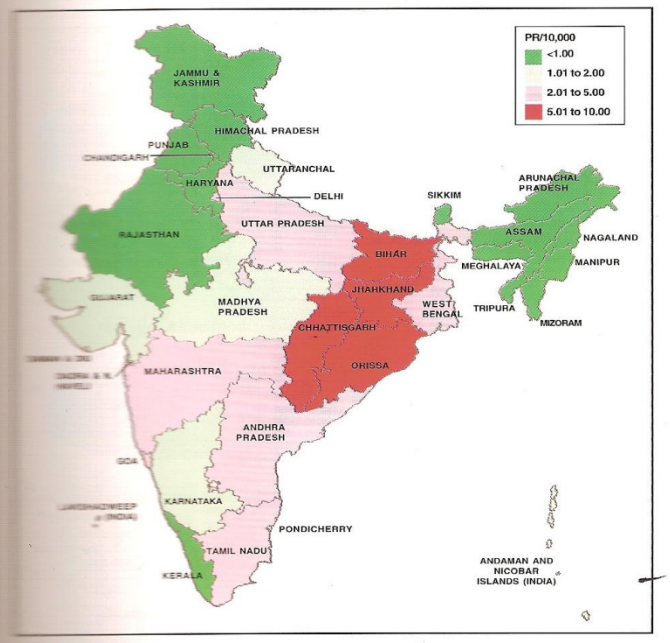
Leprosy, India by state 1981 & 2003
goal: eradication as public health problem
when prevalence < 1 pr. 10.000

Figure 1
Map of India showing state-wise leprosy prevalence in 1981



Black: > 100 pr. 10.000

Figure 3
Map of India showing state-wise leprosy prevalence in 2003



Red: >5-10 pr. 10.000

The revolutionary treatment approach: multidrug therapy by blister-packages

Leprosy situation in 2000

- In 2000, WHO announced that leprosy had been eliminated as a **public health** issue, with the global prevalence finally falling below one case per 10,000 people. This was the culmination of many years of identifying and treating patients with leprosy.
- This included the development of **multi-drug therapy – a real game-changer** in the treatment of Hansen's disease. In total, over 16 million people affected by leprosy were treated, often free of charge.

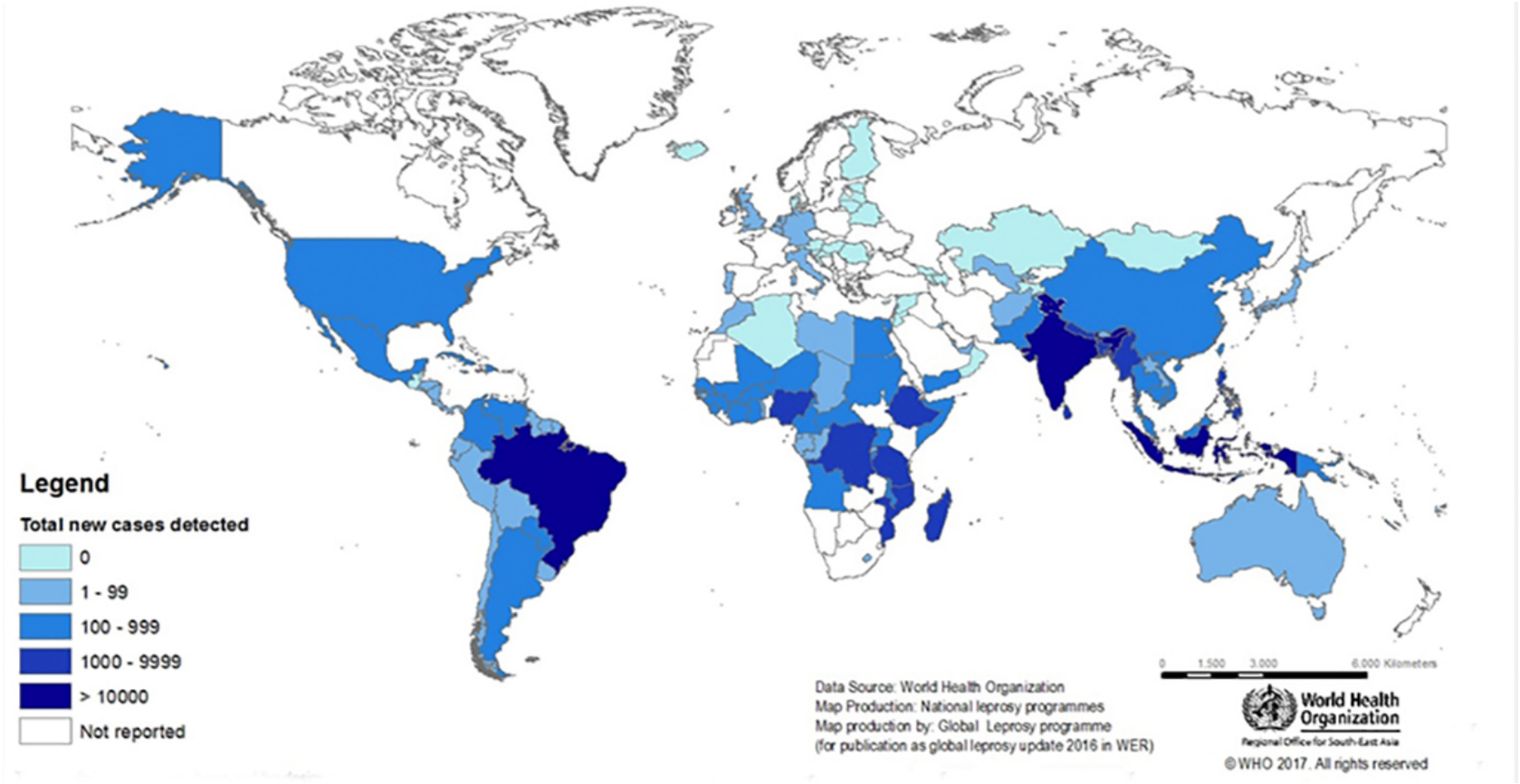
Current Situation of Leprosy in India and its Future Implications

P. Narasimha Rao and Sujai Suneetha Indian

Dermatol Online J. 2018 Mar-Apr; 9(2): 83–89.

- The **global** leprosy situation has changed significantly over the last four decades after the introduction of multidrug therapy (MDT) in 1982 with a reduction in **prevalence** from over 5 million cases in the mid-1980s to less than 200,000 at the end of 2016.
- The programme **in India** also saw a reduction from a **prevalence** rate of 57.8/10,000 in 1983 to **less than 1/10,000 by the end of 2005** when India declared to have reached the World Health Organization (WHO) target of elimination as a public health problem.

Leprosy incidence world-wide 2016



Leprosy in future

- Control by BCG vaccination (70% protect.)
- Control by Multidrug therapy, P 13 mio-> <0,3
- Control by Manipulation?: **P**revalence in relation to **I**ncidence (new cases) and **d**uration of therapy.
- P = I x d;
- decrease therapy duration x 0.5 =
  P decreased x 0.5 (”elimination” if < 10/100.000), even if Incidence not falling!

- Promising Prophylaxis:
- Rifampicin as post-exposure prophylaxis?
- Proposed re-use of Leprosaria:
- for Diabetes, cf. ulcers, neuropathy, amputations, soft shoes, blindness prevention

PEP with Rifampicin

Leprosy trial to involve 140,000 people

Teaming up with eight international partners including the Damien Foundation, ITM is gratified to be leading a new leprosy trial that will involve 140,000 people at high risk of acquiring the disease. Despite the World Health Organization's (WHO) declared elimination of leprosy - with its target of less than 1 in 10,000 people reached across the world in 2000 - the disease continues to be endemic in some countries posing a serious public health threat. Known as the PEOPLE trial - Post-ExpO-sure Prophylaxis in the Comoros and Madagascar - it looks into the optimal approach to preventing leprosy in endemic areas. This includes the Comoro islands and Madagascar, where in some areas the prevalence is 5-10 times the WHO elimination rate. The trial is generously funded by the European & Developing Countries Clinical Trials Partnership, which includes the support of the Leprosy Research Initiative.

The trial examines the antibiotic Rifampicin as a post-exposure prophylaxis. Currently this method of treating those who have been exposed to other contagious people is seen as the most effective way to stop the chain of leprosy infection. ITM and its partners are trying to find out whether the effect of prophylaxis is confined to a person's household or a broader social context.

This is in response to the WHO's call for more research into systematically tracing household contacts and finding the optimal way to administer preventive treatment for cost effectiveness reasons for healthcare systems. Fieldwork for the PEOPLE study will start early 2019, with its results hopefully also helping people with leprosy in other endemic regions.

This gentleman was successfully treated for leprosy when younger, now back for foot-care, T2Diabetes-induced

Thanks very much for your attention and your part song!