

2013-08-20-069 Leprosy - Brazil: thalidomide use, birth defects

To: (04) Mycobacterial diseases;

LEPROSY - BRAZIL: THALIDOMIDE USE, BIRTH DEFECTS

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Source: BBC News Magazine [edited] <<http://www.bbc.co.uk/news/magazine-23418102>>

A new scientific study seen exclusively by the BBC indicates that the drug thalidomide is still causing birth defects in Brazil today. It's been given to people suffering from leprosy to ease some of their symptoms, and some women have taken it unaware of the risks they run when pregnant.

Thalidomide was 1st marketed in the late 1950s as a sedative. It was given to pregnant women to help them overcome morning sickness, but it damaged babies in the womb, restricting the growth of arms and legs.

About 10 000 thalidomide babies were born worldwide until the drug was withdrawn in the early 1960s. In most countries the thalidomide children became thalidomide adults, now in their 50s, and there were no more thalidomide babies. But in Brazil the drug was re-licensed in 1965 as a treatment for skin lesions, one of the complications of leprosy.

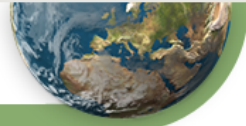
Leprosy is more prevalent in Brazil than in any other country except India. More than 30 000 new cases are diagnosed each year -- and millions of thalidomide pills are distributed. Researchers now say 100 Brazilian children have injuries exactly like those caused by thalidomide. "A tragedy is occurring in Brazil... it is a syndrome which is completely avoidable," says Dr Lavinia Schuler-Faccini, a professor at the Universidade Federal do Rio Grande do Sul. But campaigners, doctors and leprosy sufferers say the drug is vital. They believe the benefits outweigh the risks.

Schuler-Faccini and other researchers from the Universidade Federal do Rio Grande do Sul in Porto Alegre looked at the birth records of 17.5 million babies born between 2005 and 2010. "We looked at all children with limb defects and those with the characteristic defects of thalidomide," Schuler-Faccini says. We compared the distribution of thalidomide tablets with the number of limb defects and there was a direct correlation. The bigger the amount of pills in each state the higher the number of limb defects." In the same 2005-2010 period, 5.8 million thalidomide pills were distributed across Brazil. "We had about 100 cases in these 6 years similar to thalidomide syndrome," says another of the research team, Dr Fernanda Vianna. "We couldn't evaluate each case, we cannot say that all are cases of thalidomide syndrome, but this type of defect is very rare."

Poor health education and widespread sharing of medicines may [also] be to blame, she says. "[A patient] said that the doctor didn't tell him that women couldn't take it. He said they didn't tell him anything about it." There are strict regulations around the drug. It can only be prescribed to a woman who is taking 2 forms of birth control and agrees to regular pregnancy tests. There are clear warnings on the packets and there is a picture of a child damaged by thalidomide. But leprosy is a disease of the poor, in areas where health care is patchy and education is inadequate. The Amazon region, where access to the health system can be difficult, is particularly hard hit.

And plenty of people in Brazil argue that thalidomide should continue to be used. "Nowadays there is a myth about thalidomide," says Mariana Jankunas, production coordinator at FUNED, a state-owned manufacturer of the drug. "I think with information and publicity about the benefits that thalidomide brings to patients, this myth can be overcome, because the benefits outweigh the risks."

Doctors who prescribe the drug agree. "It is the best drug," says Dr Francisco Reis, from the Leprosy Clinic at Curupaiti Hospital near Rio de Janeiro. When I tell him that many people may be shocked to hear thalidomide is still being used he responds: "You have the ghosts of thalidomide in the 50s, but you should forget those ghosts." He introduces us to one of his patients, Tainah, who shows us how the medicine has reduced the debilitating lesions on her arms. "I know that I need the medicine," she tells us. She says she understands that if she doesn't take contraceptive pills she could get pregnant and give birth to a disabled child.



Brazil is a country of enormous inequalities where 20 per cent of the population live below the poverty line. Overcrowded housing and poor health systems are common to both rural areas and the slums of the cities -- places where leprosy thrives.

Where the disease is most common, thalidomide will continue to be prescribed and the risk of babies being born terribly injured will remain. Artur Custodio from Morhan, the national leprosy campaign group, recognises that the medicine is dangerous, but says it is cars that cause most injuries and disabilities in Brazil. "We don't talk about banning cars, we say we should teach people how to drive responsibly," he says. "It's the same thing for thalidomide."

[byline: Angus Crawford]

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communicated by:

ProMED-mail

<promed@promedmail.org>

[Erythema nodosum (EN) is an inflammatory immunologic reaction in the subcutaneous fat to a variety of stimuli that results in tender, red subcutaneous nodules. EN is most common on both shins, but it may also occur on other areas of the body (buttocks, calves, ankles, thighs, and arms). Conditions associated with EN include streptococcal infection, tuberculosis, sarcoidosis, histoplasmosis, coccidioidomycosis, ulcerative colitis, Behcet's disease, or drug reactions; as well as Hodgkin lymphoma, renal cell carcinoma and carcinomas of colon, pancreas and uterine cervix.

EN also occurs as an immune response to the antigens of *Mycobacterium leprae*, the organism that causes leprosy and is called erythema nodosum leprosum (ENL). ENL occurs most often in patients with lepromatous leprosy, and occasionally in borderline-lepromatous leprosy. It occurs during the course of treatment, and also occurs in untreated cases (<<http://www.iosorge.com/publications/Citations/IJL/001.pdf>>). ENL presents with sudden appearance of tender, red nodules that are often accompanied by fever; pain; general malaise; muscle, bone and joint pain; and may involve other organs, including the eyes, nerves, lymph nodes, testes, kidneys, liver, and spleen. Mild ENL may last for about 2 weeks and be followed by a reaction-free period of a month or 2; severe ENL may persist for years.

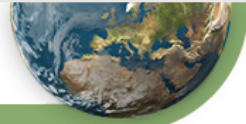
Thalidomide has been considered the treatment of choice for ENL, except in premenopausal women (<<http://www.iosorge.com/publications/Citations/IJL/001.pdf>>), because use of the drug in pregnancy is associated with severe birth defects

-- for example, missing or abnormal legs, arms, feet and hands; spinal cord defects; cleft lip or palate; absent or abnormal external ears; heart, kidney, and genital abnormalities; and abnormal formation of the digestive system. However, because of poor understanding of the risks involved by patients and perhaps health care workers, and widespread sharing of medicines, a resurgence of thalidomide-damaged babies is occurring in Brazil, as detailed in the news report above.

There are several other treatments for ENL, including the oral drugs prednisolone and clofazimine. However, a Cochrane Review of 13 randomized controlled trials that involved 445 participants and assessed betamethasone (1 trial), thalidomide (5 trials), pentoxifylline (1 trial), clofazimine (3 trials), indomethacin (2 trials), and levamisole (1 trial) found these trials were too small and poorly performed to identify important clinical differences (<<http://summaries.cochrane.org/CD006949/interventions-to-treat-erythema-nodosum-leprosum-a-complication-of-leprosy>>).

The World Health Organization (WHO) has published a statement on the use of thalidomide in leprosy (<<http://www.who.int/lep/research/thalidomide/en/index.html>>):

"Several controlled studies done in the 1970s have demonstrated that prednisolone is more effective in controlling ENL and associated neuritis. In addition, it was demonstrated that clofazimine, an anti-leprosy drug introduced on a small scale in the early 1960s, had anti-inflammatory action. Studies showed that clofazimine is the drug of choice for the management of chronic, recurrent ENL reactions, as it had both anti-reaction and anti-leprosy effects.



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"The drug clofazimine is now a component of the multidrug therapy (MDT), introduced by WHO in 1981 as the standard treatment for leprosy and now supplied free of charge to all patients worldwide. The presence of clofazimine in the combination has significantly reduced the frequency and severity of ENL reactions.

"Because of its known teratogenic [causing malformations of an embryo or fetus] effects, WHO does not recommend the use of thalidomide in leprosy. Experience has shown that it is virtually impossible to develop and implement a fool-proof surveillance mechanism to combat misuse of the drug. Today, a number of thalidomide babies continue to be born each year, reflecting regulatory insufficiency and widespread use under inadequate supervision." - Mod.ML

A HealthMap/ProMED-mail map can be accessed at:
<<http://healthmap.org/r/1zJi>>.]

[see also:

Leprosy - India: (UP) 20130716.1826562

Leprosy - Indonesia 20130222.1554276

2012

Leprosy - Pakistan: (SD) 20121222.1464477 Leprosy - India (05): (MH) comment 20120704.1189849

Leprosy - India (04): (MH) 20120703.1188726

Nigeria: (KE) 20120511.1129561

Leprosy - India (03) 20120322.1077681

Leprosy - WHO Western Pacific Region (02): background

20120217.1044390

Leprosy - WHO Western Pacific Region 20120215.1042098 Leprosy - India (02): background

20120127.1024258 Leprosy - India, Sri Lanka: persistence 20120126.1022946

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Leprosy, human, armadillo - USA: transmission 20110430.1352 Leprosy - Ghana: (TV) cases increase 20110308.0755]
