

# Thalidomide Embryopathy: A Syndrome Long Forgotten but Important to be remembered

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## Short Communication

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**Abbreviations:** MM: Multiple Myeloma; TE: Thalidomide Embryopathy; ADL: Activities Of Daily Living; DATE: Diagnostic Algorithm For Thalidomide Embryopathy.

## Short Communication

I have been heading up the official group to support and examine thalidomide victims funded by Ministry of Health, Labour and Welfare in Japan for several years. Today it is well known that thalidomide and its derivatives came into the spotlight because they were well recognized to have favorable effects for leprosy, multiple myeloma (MM) and a few other diseases [1]. Consequently, thalidomide was approved and licensed around the world, and it is currently used in many countries.

However, thalidomide also has a historically dreadful side not to be forgotten, thalidomide embryopathy (TE) caused by the oral intake of thalidomide during pregnancy. TE has been one of the most striking medical disasters after the 2<sup>nd</sup> World War. Thousands of babies with birth deficits and impairments, such as phocomelia, abnormally short arms, hearing impairment, organ malformations and other birth deficits were born in many countries from 1958.

Thalidomide, a kind of sedative and hypnotic, was first developed and sold as a safe medicine in Western Germany in 1956 [2]. At that time, it was sold in more than 40 countries throughout the world and preferably taken by some pregnant women for morning sickness or

insomnia, not knowing of its risk of teratogenicity. Consequently, thalidomide intake not only induced thousands of births with TE, but nearly half of these babies died shortly after birth and in early infancy. The sale of thalidomide was discontinued in several developed countries and in other countries in the early 1960's after the etiology of TE was disclosed.

Some may think that all of the problems associated with TE have already been resolved. However, this is far from the truth, as many problems of TE still remain to be resolved. Notably, I should take up two problems here. First, it has been reported that many babies with birth deficits, likely induced by thalidomide, were found in Brazil even after the 1960's [3]. Thalidomide has still been available in some districts of Brazil with endemic leprosy. Actually, Brazil approved use of thalidomide for the treatment of erythema nodosum leprosum in 1965 [4]. In short, thalidomide has been easily obtainable and may be taken by younger pregnant women who are unaware of its risk. We can imagine that the use of thalidomide was not perfectly controlled in some endemic regions with leprosy in Brazil. This is thought to be the reason why new babies with TE were born in the 1970s through 1990s [3]. Consequently, new cases with TE have been repeatedly reported from Brazil. There might also be some new cases with TE in a few other developing countries.

Moreover, we must think of new claimers for TE as well. We have been facing new claimers, particularly those in the developed countries that insist their anatomical deficits and/or hearing impairment were caused by thalidomide. For example, I learned there have been 105 new claimers for TE in Germany between 2009 to 2017. Only 10 new claimers have been approved to be

real thalidomide victims. More than half of 105 claimers have never been recognized as thalidomide survivors. I heard from the Thalidomide Trust in 2018 that there had been more than 200 new claimers in UK, and only a small number of them were accepted as real thalidomide victims. We have annually had a few new claimers for TE in Japan, too. I think there are some reasons why many people with limb deficits and/or hearing impairment still claim that they are thalidomide victims. Most of them do not know for sure whether or not their mothers took thalidomide in their pregnancy. We could not demonstrate if their mothers took it or not, dating back to more than half a century. Usually there remains no evidence available in most cases as to whether they took it. It can also be suspected that some of the new claimers want to receive any compensation, pension or living expenses because they have been suffering from impaired ADL (activities of daily living) and pains, whatever the real cause they may be. Indeed, such symptoms might originate from real TE in a limited number of cases, but are presumably caused by other congenital diseases or acquired problems in most cases. In Brazil, for example, TE and its similar birth deficits caused by other reasons might coexist as well.

Conclusively, TE is not a serious drug tragedy of the past, but rather an ongoing problem to be resolved. In fact, there are many thalidomide survivors living and struggling with various disabilities and obstacles in many countries. I know that many groups, public or private, are vigorously supporting thalidomiders and considering how to treat them in developed countries, such as Germany, UK, Sweden and Japan; this is a greatly significant work. Considering the above situation, especially the new cases of TE in Brazil and new claimers in developed countries, we have finally reached another big theme in TE in that we should determine the diagnosis criteria for TE. Previously, WHO attempted to settle the diagnosis criteria, and recently a UK group just showed a diagnostic algorithm for thalidomide embryopathy (DATE) [5,6]. Our Japanese research group will soon be starting to make the

diagnosis criteria for TE specific to Japan. We will hold the 2nd International Symposium on TE in Tokyo on July 14 and 15, 2019. At that time, the diagnosis criteria for TE will be discussed among many experts from UK, Germany, Sweden, Brazil and Japan. I think it is hard to design the perfect criteria which can be appropriately used in every country because the grades and types of deformities, the physical expressions, distribution of the upper-limb type, the hearing impairment type and the mixed type, and other pathological situations greatly differ by country. However, I think it meaningful to discuss and deeply consider how to diagnose TE internationally and to finally make the appropriate diagnosis criteria, fitting the real situation and the physical and medical problems in each country after a lively international discussion.

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