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A Short History of Thalidomide Embryopathy

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Immediately following the first synthesis of thalidomide, and patent application, clinical trials with thalidomide were started in April 1954. The substance was tested for spasmolytic, local anesthetic and anticonvulsive effects. It was supposed to have antihistamine and antiergotropic activity as indicated by its German name Contergan. When thalidomide was tried in three women with spastic constipation, it was unexpectedly found to induce sleep. Clinical trials included patients with vegetative dystonia, tuberculosis, influenza, pertussis, hypertension, atherosclerosis, hyperthyroidism, gastric complaints of nervous origin, and liver disease. In November 1956, thalidomide was marketed under the name of Grippex, indicating that it was supposed to be helpful against "Grippe", i.e., influenza. In August 1956, a leaflet was printed enumerating the following indications: irritability, weak concentration, stage fright, ejaculatio praecox, menstrual tension, postmenopausal symptoms, fear of examination, functional disorders of the stomach and gallbladder, febrile infectious diseases, mild depression, anxiety, hyperthyroidism, and tuberculosis. The claim was raised and maintained for several years that such a multipotent drug was virtually free from side effects.

In November 1957, Contergan was launched on the market, supported by an effective propaganda campaign. At that time it was well known that many chemical substances, including some with low acute toxicity in adults, might damage the fetus. By 1950, Ancel, in his monograph "La Chimioteratogénèse, Réalisation des Monstruosités par des Substances Chimiques chez les Vertébrés," had analyzed the results of experiments reported in 490 published papers. In 1958, Willis, in his book "The Borderline of Embryology and Pathology," stated: "It will be noted that only a few chemical agents have yet been tested for teratogenic effects in mammals, and that these do not include any of the commonly used alkaloids, sedative drugs, sulphonamides, antiseptics, dyes, organic solvents, or metallic and other inorganic substances. Methodical investigation of the effects of all of these on early mammalian development is needed." This opinion was based on facts known prior to 1957. Out of 15 papers quoted in Willis's chapter "Chemical Poisons as Causes of Malformations," 14 had been published before 1955, and only one in 1957. Similar statements as Willis's abound in the scientific and more practice-oriented medical journals of the 1950s.

The assertion that nobody could have foreseen in 1956 a tragedy such as that caused by thalidomide does not become true by reiteration. As I am not competent to judge the various ethical and juridical problems laid open by the thalidomide tragedy, my paper is limited to facts selected for their bearing on the responsibility of doctors, scientists, drug companies, governmental agencies, and legislators.

The papers published in 1956 by Kunz et al. on animal experiments and by Jung on clinical experiences with thalidomide have so little scientific value that in my opinion they should not have been accepted for print (for a critical comment see Lenz, '79). The publishing of papers on new drugs is one of the main links in the chain of events leading to their marketing, which should be carefully controlled. Too many doctors are naively believing in the therapeutic effects of chemicals. In the face of the amount of human suffering, the unsatisfactory state of treatment of many diseases, and the pressing demand of the public for cures, it is understandable that many doctors prescribe the pills in which they happen to believe. Doctors, I believe, should not compete with shamans and quacks and should remember the presidential address by the late Professor Lawson Wilkins of Johns Hopkins before the American Pediatric Society in May 1962: "Finally I feel that one of the great shortcomings of our medical teachers of the present generation is a failure to inculcate

into students and interns a cold, scrutinizing, skeptical state of mind which would make them wary of accepting any therapeutic claim without proof. If the young physician were less credulous and gullible he would be less enthusiastic about trying every new sample of the 400 new drugs handed to him annually, and he might do less damage to his patients . . . Remember that practically every effective and worthwhile drug has potentials for toxic or undesirable side effects. Weigh carefully its advantages against the possible risks."

In a statement read at the 1962 meeting of the American Academy of Pediatrics in Chicago and published in the supplementary exhibits to the Hearings of the U.S. Senate Committee on Interagency Coordination in Drug Research and Regulation (1963) I said: "It will probably never be possible to prevent with certainty any harmful effects of drugs. The following principles, however, might contribute to reduce the damage:

1. Any drug treatment is an experiment involving a certain risk.
2. The effects of drugs on the embryo are largely unexplored.
3. In any medical case history the drugs that have been taken should find a place. Drugs taken during pregnancy should be noted as a routine in obstetric and pediatric history taking.
4. It would be desirable if patients knew which drugs they have taken.
5. Doctors should keep notes of all drugs they have prescribed or distributed as samples.
6. All drugs given in the hospital should be entered on the case sheet.
7. All drugs that are put on the market should at first be sold only on prescription. Some drugs might after due time be released for sale over the counter.
8. Any suspicion of side effects of drugs should immediately be communicated to the producers as well as to an independent committee for further investigation. The responsibility to withdraw a drug should not be left to the producers.
9. Known side effects should be clearly stated on the circulars accompanying the packages.
10. If there are side effects, the patients should be told.
11. Pharmaceutical firms should be made legally responsible if they publish or promote false statements as to the effects of drugs or suppress or delay publication of information on harmful effects.
12. Printed material distributed by pharmaceutical firms should not be taken as scientific information.
13. At some places sampling registration of malformations should be instituted and evaluated at short intervals. More extensive population studies may be desirable for other purposes, but are too time comsuming to be of much value for rapid detection of important changes in the incidence of malformations. Epidemics of malformations should be considered at least as urgent as epidemics of contagious disease.
14. The optimistic faith in the magic power of the most recently introduced pill should give way to a more realistic attitude. Never should any drug be given only to make the patient feel that something is done."

Certainly, conditions have improved since, but my statement has not become entirely obsolete. There still is and probably will remain a genuine conflict between the interests of the producers and the consumers of drugs. Given the financial power of the drug companies and the amount of money spent in advertising, nothing short of deliberate resistance by medical doctors, state agencies, and the press will be sufficient to offer some sort of delicate balance.

In Table 1, the months of birth of 3,049 thalidomide children born in the Federal Republic of Germany are shown. The first known case was a girl born December 25, 1956, at Stolberg, the place of Grünenthal Chemie. The father, who was working for the company, received samples of the new pill for his wife. The girl had no ears. A few more cases can be attributed to samples distributed before the marketing of thalidomide, but the epidemic became conspicuous only about 1 year later, and it closely followed the monthly sales figures by a distance of about 7–8 months, as expected if

the sensitive period is considered. In Sweden, thalidomide was introduced in September 1958, and, as a consequence, the Swedish epidemic started only late in 1959. In Brazil, thalidomide was not sold before March 1959, the epidemic following in the first half of 1960. In Ireland, thalidomide was first marketed in May 1959, but only very small amounts were sold before June 1960, so the epidemic did not start prior to 1961. In Canada, thalidomide was put on the market in April 1961, and the dysmelia epidemics did not start before December 1961 (Webb, '63). The end of the epidemic likewise depended on the time the drug was withdrawn. There was, as expected, a sharp fall of the German epidemic in July and August, roughly 8–9 months after the withdrawal of thalidomide by the end of November 1961. In Brazil, thalidomide continued to be widely sold up to June 1962, and the epidemic ended about half a year later than in Germany. Similary, in Japan, sales of thalidomide went on throughout 1962, so that 52 cases were born in 1963 or later. If cases in which thalidomide was taken after the time when the drug had been removed from the market in Germany are called avoidable, then there are 15 avoidable cases in Brazil, 110 in Japan, 5 in Sweden, and 81 in Germany.

The halt to the sale and the warnings sent out by the producers in some countries were not entirely effective. Governmental agencies were hesitant. The press was clearly the prominent factor not only in forcing the reluctant companies in West Germany, Canada, and Japan to withdraw the drug, but also in communicating the danger to the public. In 1961, the legal system of most countries was not prepared to meet such a tragedy. It tolerated the producer's refusal to take notice of the available facts and to continue for a long time the spread of misinformation. The incomplete information communicated from Grünenthal to the Japanese Dai-Nihon-Company was instrumental in thalidomide's continued advertising in Japanese newspapers until the summer of 1962 as a sleeping pill with no side effects.

An estimate of the total figure of thalidomide embryopathy may be arrived at by the following argument: I have collected files of 3,773 cases that can be attributed to thalidomide with reasonable certainty from both pregnancy histories and morphology. Although false-positives are not excluded with absolute certainty, they constitute probably less than 1%. This material includes most surviving patients in the countries included in the German recompensation scheme, i.e., the Federal Republic of Germany, Austria, Belgium, Finland, Ireland, The Netherlands, Portugal, Spain, Switzerland, and several Asian, South American, and Meso American countries. Some of the Swedish cases also are included, as are the cases from Japan and Taiwan. Only a minority of cases from the United Kingdom, Italy, Denmark, Norway, Canada, and Australia are in my files. From various sources the true number of surviving cases may be estimated to comprise about 400 cases from the United Kingdom and probably more than 200 cases from other countries not included in the German and Japanese recompensation schemes. Therefore, the total figure would be around 4,400 cases of which 498 are deceased, leaving some 3,900 surviving cases. The mortality of thalidomide children was probably around 40%, so the 3,900 surviving cases represent about 60% of an original total of 5,850. Though esti-

TABLE 1. Thalidomide cases: Germany[1]

Month	1956	1957	1958	1959	1960	1961	1962	1963	1964	1965	1966	1967
I			1	6	16	73	152	3				
II			1	2	19	83	131	1	1			
III		1		5	18	108	138	2				
IV			1	7	21	106	149	1		1	1	
V			1	9	31	124	127					1
VI			2	8	41	143	95					
VII				8	32	134	68	2				
VIII			4	6	45	133	34					1
IX			4	13	59	170	10					
X			1	10	63	159	7					
XI			4	9	46	158	10					
XII	1		5	14	59	144	6					

[1]Avoidable cases (born August 1962 or later): 81. Total cases: 3,049.

TABLE 2. Thalidomide embryopathy and mortality

Location	No. of cases	No. died	% died
Sweden	153	66	43
Hamburg	121	46	38
Canada	116	41	35
The Netherlands	25	9	36
Total	415	162	39

mates of the mortality appear to be rather consistent for Western Germany, Sweden, and Canada (see Table 2), neonatal mortality was possibly higher in some other countries. Thus, in Japan, Dr. Kajii ('62) has estimated the mortality to have been about 80%. I have personally seen abandoned children with severe limb defects in various institutions in Hong Kong, Taiwan, and Tokyo. In some countries, until quite recently, malformed infants have usually been left to die because of the belief that they were something devilish, created by bad demons.

On the other hand, the European estimates of mortality might be too high, as they probably refer to the more conspicuous cases. Minor malformations of thalidomide tended to be overlooked for a considerable time. There is, in addition, strong though circumstantial evidence that thalidomide taken at high doses throughout the sensitive period might induce abortion. If these aborticns were known, they might greatly increase the total number of fetal damage by thalidomide, possibly by a factor of 2 or more.

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Jung, H. (1956) Klinische Erfahrungen mit einem neuen Sedativum. Arzneim. Forsch., *6*:430–432.

Kajii, T. (1962) Thalidomide and congenital deformities. Lancet, *2*:151.

Kunz, W., Keller, H., and Mückter, H. (1956) N-phthalyl-glutaminsäure-imid Experimentelle Untersuchungen an einem neuen Synthetischen Produkt mit Sedativen Eigenschaften. Arzneim. Forsch., *6,8*: 426–430.

Lenz, W. (1979) Thalidomide facts and inferences. In: Drug-Induced Sufferings. Int. Congr. Ser. No. 513. Proc. Kyoto Int. Conf. Against Drug-Induced Sufferings, Kyoto, pp. 103–109.

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Willis, R.A. (1958) The Borderland of Embryology and Pathology. Butterworths, London.

APPENDIX: THALIDOMIDE EMBRYOPATHY IN VARIOUS COUNTRIES

The numbers of thalidomide cases are minimal estimates of the total numbers, since stillborn infants and early deaths are underrepresented, and the ascertainment of the surviving cases is probably very incomplete in some countries. The figures given for thalidomide sales are compiled from various sources, such as communications by the producers, material presented to the German law court, and estimates given by the National Ministries of Health. The literature quoted selectively refers to typical cases described in detail and to epidemiological surveys. No attempt is made to cover the extensive literature. Illustrative cases from the Muenster register of limb malformations are presented for some countries.

Australia: Thalidomide embryopathy cases: 26

Some of these cases are apparently not due to thalidomide

Thalidomide sales figures: not known 1960–December 1961 (1962?)

McBride, W.G. (1961) Thalidomide and congenital abnormalities (Letter to the Editor). Lancet, *2*:1358.

McBride, W.G. (1963) The teratogenic action of drugs. Med. J. Aust., *2*:689–692.

Short tabulation of 14 cases with typical malformations following intake of thalidomide; 8 of these died.

Austria: Thalidomide embryopathy cases

1960	2
1961	3
1962	2

Thalidomide sales

1960	72 kg
1961	127 kg

Rett, A. (1965) Das Thalidomidproblem in Österreich. Wien. Med. Wochenschr., *115*: 21–28.

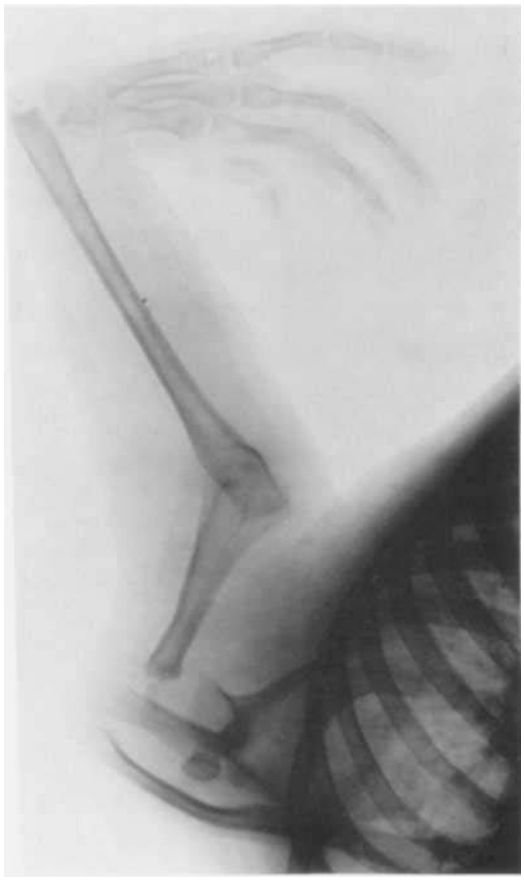

Fig. 1. X-ray at age 9-3/12 years. Left arm: short humerus, aplasia of the radius and thumb, rudimentary second finger. On the right arm (not shown), the findings are essentially similar, only the humerus is somewhat longer and there is a slender second metacarpal of about normal length. The patient has been operated on for pyloric stenosis. Distaval in pregnancy. Australia.

Belgium: Acknowledged thalidomide embryopathy cases

1959	3
1960	12
1961	6
1962	14

Thalidomide sales

1960	97 kg
1961	163 kg

Heynes, D. (1963) Premiers éléments statistiques relatifs aux malformations congénitales en Belgique. Arch. Belg. Méd. Soc., *21*:186–198.

Brazil: Acknowledged thalidomide cases

1959	1
1960	27
1961	29
1962	39
1963	2
1978	1*

*Mother treated for leprosy.

Thalidomide sales: unknown, various pharmaceutical firms involved
March 1959–June 1962

Schmidt, M., and Salzano, F.M. (1980) Dissimilar effects of thalidomide in dizygotic twins. Acta Genet. Med. Gemellol., *29:* 295–297.

Among 93 Brazilian cases of thalidomide embryopathy, the authors found one pair of (dizygotic) twins. The mother has had Slip during the first 3 months of pregnancy. One twin had aplasia of the right radius and thumb, the other one a triphalangeal thumb on the left hand and duodenal stenosis (no description of the contralateral limbs of the twins).

Canada: Thalidomide embryopathy cases
115 (estimate by Webb, 1963; revised estimate, Webb, 1965) 122 infants born to 119 mothers (3 sets of twins) who had received thalidomide; 40 additional infants had typical malformations, but drug intake could not be confirmed (some of the mothers probably had thalidomide)

Thalidomide sales
April 1, 1961–March 2, 1962: total amount not known

Webb, J.F. (1968) Canadian thalidomide experience. Can. Med. Assoc. J., *89*:987–992; *92*:585–586, 1965; personal communication.

Denmark: Thalidomide embryopathy cases: 20

Thalidomide sales figures

	Import	Total sales
1959	3 kg	
1960	17 kg	147 kg
1961	27 kg	

October 1959–December 1961 (1962?)

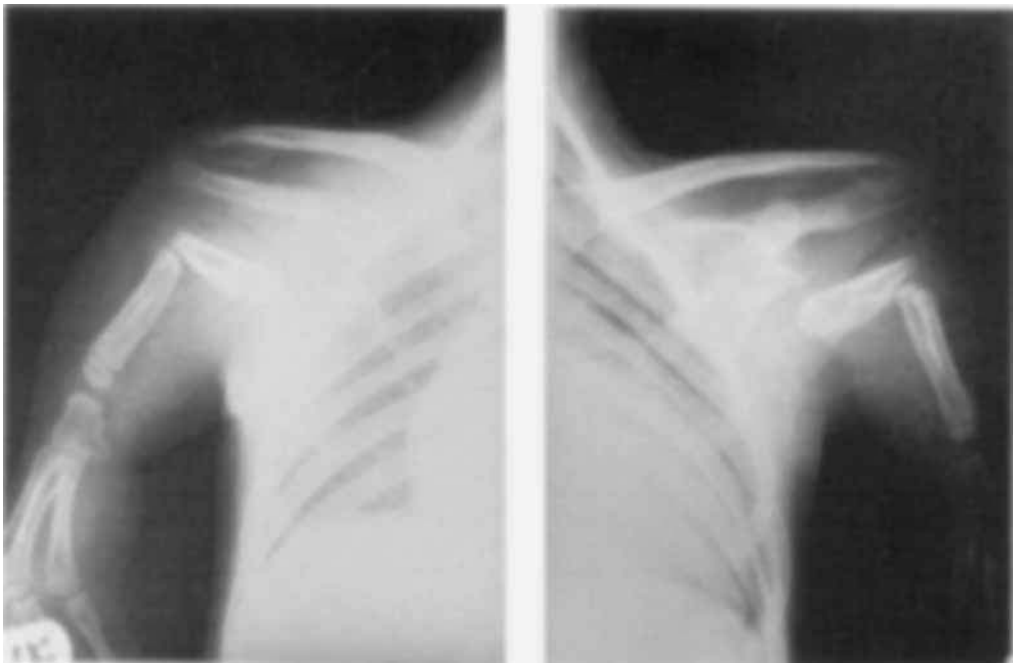

Fig. 2. Prescriptions of Softenon forte (100-mg tablets) on October 16 and November 7, 1961. Last menstrual period on April 5, 1962, intake of tablets on May 1962. Bilateral aplasia of thumb and index finger. Bilateral coloboma of chorioidea. Belgium.

Heg, E. (1962) Neosedyn-misdannelser. Ugeskr. Laeg., *124*:548.

Lütken, P. (1962) Neosedyn-misdannet barn iagttageti Denmark. Ugeskr. Laeg., *124*:367.

Thiele, S. (1962) Talidomidmisdannelser. Ugeskr. Laeg., *124*:1250–1251.

Aplasia of humerus and radius, three fingers on each side. Aplasia of femurs and tibiae. Neosedyn, five to eight tablets.

Federal Republic of Germany: Thalidomide embryopathy cases

1956	1*
1957	1*
1958	24
1959	97
1960	450
1961	1,515
1962	927
1963	9
1964 and after	5

November 1957–November 1961

*Cases following intake of premarketing samples. Small amounts of the thalidomide-containing drug Grippex had been marketed in 1956.

Thalidomide sales and samples in kg

1957	33
1958	728
1959	3,800
1960	14,580
1961	11,060

Lenz, W., and Knapp, K. (1962) Thalidomid-Embryopathie.
Dtsch. Med. W., *87*:1232–1242.

Finland: Thalidomide embryopathy cases

1960	2*
1961	0
1962	6

*One case born in March, father a medical doctor, received samples of Softenon. One

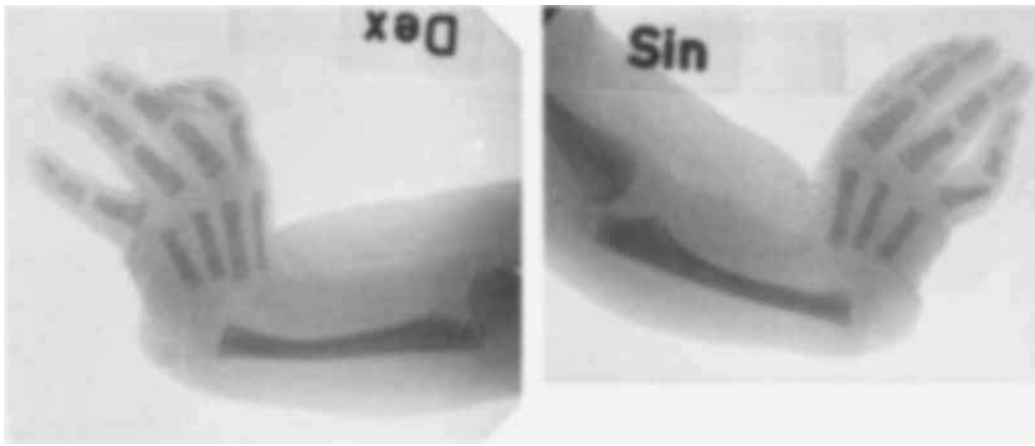

Fig. 3. The father, who is a medical doctor, got samples of Softenon in the summer of 1959. Finland.

case born April, mother a nurse, received Softenon at hospital where she worked.

Thalidomide sales: 67 kg
September 1959–December 1961

Väänänen, I., and Joki, I. (1963) Two cases of phocomelia in Finnish Lapland. Ann. Paediatr. Fenn., *9:*65–71.

Ireland: Acknowledged thalidomide cases

1959	1
1960	0
1961	13
1962	20
1963	2

Northern Ireland: 15 cases
Thalidomide sales
May 1959–January 1962

1959	3 kg
1960	27 kg
1961	97 kg

Enterosediv powder not included, as data on sale are not clear.

Italy: Thalidomide embryopathy cases

1961	22
1962	59
1963	5

Thalidomide sales

1960	126,000 applications
1961	195,000 applications
July 1962	90,000 applications

(exact doses not indicated)
1960–July 16, 1962 (ceased by decree of Ministry of Health)

Gomirato-Sandrucci, M., and Ceppelini, R. (1962) Considerazioni cliniche e patogenetiche su alcuni casi di focomelia. Min. Ped., *14:*1181–1202.

Torbidoni, L., Catana, G., Di Iulio, and Save, F. (1967) Le malconformazioni congenite attraverso dieci anni: Andamento delle aplasie degli arti con particolare riguardo alla c.d. embriopatia talodimidica. Ann. Sanita Pubblica, *28:*1–53.

Lenz, W. (1970) Übersetzungsfehler, falsche Zitate und Widersprüche. Dtsch. Ärzteblatt, *67:*2725–2729.

Japan: Acknowledged thalidomide embryopathy cases (incomplete number)

1959	16
1960	19
1961	59
1962	153
1963	45
1964 and after	7

Thalidomide sales: total amount not known
January 20, 1958–September 13, 1962

Tabuchi, A., Yamada, A., Umisa, H., Shintani, T., Horikawa, M., Shirasuna, K., and Sawasaki, M. (1963) Phocomelia-like deformity and thalidomide preparations. Hiroshima J. Med. Sci., *12:*11–35.

Fig. 4. Left arm (not shown): almost exactly the same radiological findings as on right arm. Softenon was prescribed before pregnancy. Ireland.

Detailed report on five living and five stillborn children, including a pair of dizygotic twins with concordant hypoplasia of the humerus and aplasia of the radius. Photographs of three cases.

Takemori, S., Tanaka, Y., and Suzuki, J.-I. (1976) Thalidomide anomalies of the ear. Arch. Otolarynogol., *102*:425–427.

Fifteen cases of thalidomide damage to the ear examined at Teikyo University, Tokyo. Only one of these cases had limb malformations in addition. Five cases presented in detail.

Mexico: Acknowledged thalidomide embryopathy cases

1961	3
1962	1

Thalidomide sales: 156 kg
Withdrawn early 1962

Mateos Cándano, M. (1963) Un caso de sindrome talidomidico. Ginec. Obstet. Mex., *18*:73–85.

First case of thalidomide embryopathy published in Mexico was born on September 5, 1962. The author was aware of several unpublished cases. Talargan, 12 tablets of 100 mg; intake started before last menstrual period.

Right arm: humerus fused with radioulnar synostosis, three metacarpal bones, three fingers, each has three phalanges. Left arm: similar angulated humeroradioulnar synostosis as on right arm, three metacarpal bones, aplasia of the thumb, osseous syndactyly 1 + 2. No internal malformations (autopsy, child died on first day).

The Netherlands: Thalidomide embryopathy cases

	Surviving acknowledged	Geneeskundige Hoofdinspectie*	
1960	5	7	9 cases died
1961	4	8	
1962	8	10	

*Total number possibly is incomplete, as only 88.7% of the doctors returned the questionnaires, and as the completeness of the returned questionnaires is doubtful.

Thalidomide sales (Softenon, Enterosediv, Noctosediv)

1959	16 kg
1960	47 kg
1961	46 kg

January 1959–November 1961

Fig. 5. Bilateral distal rudiments of humerus, total radioulnar synostosis. Left hand: first and second ray missing. Right hand: first ray missing, rudimentary second ray. X-ray at age 5-10/12 years. Mother took Imidene. Italy.

In addition, 26–30 kg/year as doctors' samples
In November 1961, about 20 kg was withdrawn from the market and destroyed
GHI Bulletin: January 1963!

Thalidomide Misvormingen in Nederland, pp. 1–20.
Den Haag. Geneeskundige Hoofdinspectie.

Norway: Thalidomide embryopathy cases: 11
Thalidomide sales
1959 2 kg
1960 36 kg (42)
1961 51 kg (61)
November 1959–December 1961

Kvaale, K. (1962) Iatrogen Misdannelse. Tidsskr. Nor. Laegeforen., pp. 907–908.
Sundal, A. (1962) Iatrogen Misdannelse. Tidsskr. Nor. Laegeforen., pp. 379–380.
Vaage, S., and Berczy, J., (1962) Iatrogene Misdannelser. Tidsskr. Nor. Laegeforen., pp. 1202–1206.
Tabulation of nine cases of limb malformations and one case of anotia; three born in 1961, seven born in 1962.
Neurodyn intake in eight cases, doubtful in an additional case. Four cases died.

Spain: Acknowledged thalidomide embryopathy cases
1961 3
1962 2 (1 case Contergan bought in Federal Republic of Germany)

Thalidomide sales: total amount not known May 1961–May 1962 (?)

Carbonell Juanico, M., Bolonjo Cabot, E., Trias de Bes, J.M. (1962) Considerations on two cases of phocomelia. Embryopathy caused by thalidomide. Rev. Esp. Pediatr., *18*:607–705.

Sweden: Cases of thalidomide embryopathy

	Weinberg, 1964 Skeletal malformations thalidomide type	Winberg, 1986 Acknowledged surviving cases
1959	not covered by survey	3
1960	37	31
1961	58	37
1962	52	33
1963	not covered by survey	2
1964	not covered by survey	1

Fig. 6. Prescription of Talargan, March 15, 1960. Bilateral aplasia of the humerus, radius, thumb, and second finger. Mexico.

Fig. 7. Softenon and Noctosediv were prescribed. The Netherlands.

Thalidomide sales
1959 171 kg
1960 246 kg
1961 284 kg
September 1958–December 1961

Bergström, A.L., Nilsson, L., Petterson, G., Söderling, B., Victorin, L., and Winberg, J. (1962) Talidomid Embryopati. Sven. Laekartidn., *59:*1012–1022.
Detailed description of five cases from Göteborg and seven cases from Boräs. Five cases shown by photographs and X-rays. Details on thalidomide intake. Six cases died, six survived. These cases are in no way different from those observed in Western Germany.
Winberg, J. (1964) Utredning Rörande det Eventuelle Sambandet mellan Fosterskador och Läkemedel. Sven. Laekartidn., *61:*718–741, 814–831, 890–902.
Detailed epidemiological study of Swedish thalidomide cases. In addition to the skeletal malformations, ten cases of anotia born from 1960 to 1962 and associated with maternal thalidomide consumption were registered. Four cases of skeletal malformations born from September to December were still associated with thalidomide intake.

Fig. 8. Five tablets of Neurodyn during the first weeks of pregnancy were prescribed before conception. Aplasia of the tibiae. Norway.

Fig. 9.**a:** Softenon was prescribed in early March 1960. Ingenital hernia, strabism. **b:** X-rays of the left arm, July 31, 1980, at age 18-8/12 years. Right arm (not shown): aplasia of the first and second ray. Both arms: short distal rudiment of the humerus. Spain.

Switzerland: Acknowledged thalidomide embryopathy cases
1961 6
1962 6

Thalidomide sales
1960 22 kg
1961 91 kg
September 1958–December 1961

Werthemann, A. (1963) Allgemeine und Spezielle Probleme bei der Analyse von Missbildungsursachen, in Sonderheit bei Thalidomid und Aminopterinschäden. Schweiz. Med. Wochenschr., *93*:223–227.
Mother took Softenon from the 41st to the 45th postmenstrual day, 75 mg/day. Baby was born with no left arm, and a hand with two fingers attached to the right shoulder. Renal cysts, bilateral megaureter, cryptorchidism.

Taiwan: Acknowledged thalidomide embryopathy cases
1960 8
1961 5
1962 10
1963 4
1964 and after 9
(36 surviving cases according to Yang et al., 1977)

Isomin, Proban M.: 1958–September 6, 1962 total sales not known

Yang T.S., Shen Cheng, C.C., and Wang, C.M. (1977) A survey of thalidomide embryopathy in Taiwan. J. Formosan Med. Assoc., *76*:546–562.
Photographs and X-rays of ten cases are shown (phocomelia, triphalangy of thumbs, anotia). Tabulation of malformations.

United Kingdom: Ministry of Health Report on Public Health and Medical Subjects No. 112
Deformities caused by thalidomide: London. Her Majesty's Stationary Office, 1964
Covering only children born between January 1, 1960 and August 31, 1962
Children with limb malformations whose mothers certainly (237) or probably (112) had thalidomide

Year	No.	Thalidomide sales in period 9 months prior to periods of birth
1960	49	1,170 kg
1961	97	2,660 kg
1962	125	2,530 kg
Total	271 (201 living, 70 dead)	

From the figures for dead children, no estimate of the mortality should be derived since the information on live-born children who died prior to the completion of the survey is likely to be incomplete. The total number of malformed babies whose mothers certainly had thalidomide was 237, that of those whose mothers probably had thalidomide was 112. There were 42 cases of ear malformations with no mention of limb malformations, in which the mothers had certainly or probably had thalidomide. In addition, there were 366 malformed children where there was no indication that their mothers had taken thalidomide. "There is little doubt that at least some of the malformations in group III (i.e., no indication of thalidomide) were the result of thalidomide." There was one child born in 1963 with bilateral malformations of the upper limbs. The mother took a thalidomide product.
Marre, A. (1978) By 1978 Distillers Company had accepted 435 cases from the United Kingdom as thalidomide damaged. Total sales of thalidomide in the United Kingdom amounted to 5,769 kg. Sales started in April 1958 and were stopped in December 1961.
Marre, A. (1978) Thalidomide "Y" List Inquiry. Report of the Department of Health and Social Security. Her Majesty's Stationary Office, London.

Portugal: Acknowledged thalidomide embryopathy cases
1961 2
1962 6
Thalidomide sales: 36 kg (practically only in 1961)
August 9, 1960–December 14, 1961

According to a communication by the Portuguese Ministry of Health and Assistance, medical samples were used more than the drug put on the market.

Fig. 10a and b. England.

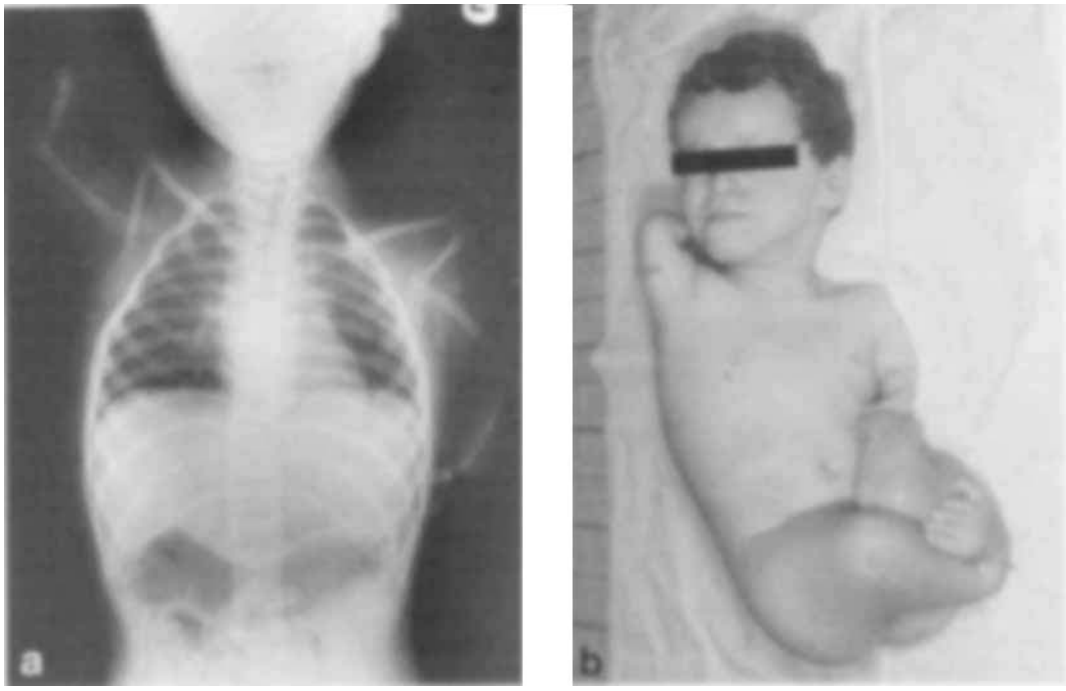

Fig. 10c. Deafness, anophthalmia. Distaval from 43rd to 48th postmenstrual day. Total amount: 700 mg.