CHAPTER 11

Unruly Bodies, Unruly Statistics: Thalidomide and the Birth of Reproductive Epidemiology in the Early 1960s

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In 1964 Sweden's National Board of Medicine decided to make permanent the Register of Congenital Malformations. This meant that from January 1, 1965, any congenital malformations were to be reported to the board's statistical department, and the newly formed Register of Congenital Malformations.[1] The aim of founding the register was that it would serve as an early warning system against fetal damages—whatever the source may be. The plan was that the register would be able to detect any increase in the number of infants born with congenital malformations, and any new patterns to these abnormalities.[2]

The decision to track congenital malformations in Sweden was, as in many other countries, a consequence of the thalidomide tragedy, in which almost six thousand infants were born with grave malformations globally.[3] The drug thalidomide was introduced in the late 1950s and was often prescribed for morning sickness in pregnant women. It was marketed in forty-six different countries under various names. In Sweden, thalidomide was introduced on the market in early 1959, and sold under the names Neurosedyn and Noxodyn. The birth defect epidemic caused by the drug consequently started in late 1959 in Sweden.[4]

This chapter deals with the events leading up to the foundation of the Register of Congenital Malformations, and the practical struggles to produce knowledge about unknown patterns of malformations through the statistical surveillance of birth defects. It investigates the tension between surveilling for unknown

1 Swedish Code of Statutes in the Field of Health and Sick Care, 'Kungliga Medicinalstyrelsens cirkulär.'

2 A note about the language of defects and malformations. In the chapter I use the words 'birth defects' and 'congenital malformations.' These words are both used in medical practice today, and I use them to reflect the medical language that I am trying to portray. See for instance Carachi and Doss, *Clinical Embryology*, which has the subtitle *An Atlas of Congenital Malformations*, and Singh, 'World Birth Defects Day.'

3 Lenz, 'Short History of Thalidomide Embryopathy'; Bergström et al., 'Talidomid-embryopati.' See also the chapter by Björkman in this volume.

4 Lenz, 'Short History of Thalidomide Embryopathy'; Bergström et al., 'Talidomid-embryopati.'

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abnormalities and standardized reporting, through the lens of the surveillance of congenital malformations. To do this, the chapter deals with the prehistory and the early days of the Register of Congenital Malformation and the challenges of using statistical methodologies for disease surveillance. The chapter seeks to analyze the practices of detecting unknown syndromes through the reporting of congenital malformations—which stands in contrast to medical practices of diagnosis using standardized categories of disease.

The aim of this chapter is to contribute to the history of Nordic epidemiology and disease surveillance. However, rather than focusing on epidemiological registry practices, such as linking records through unique identifiers, or the work of repurposing data from large-scale social and medical registries, this chapter approaches registry-based research from the point of view of the practices of classification.[5] It highlights how medical practitioners and statistical researchers struggled to standardize and bring under control that which belied the normal—their work to circumscribe, value, categorize, and track abnormalities in practice.

The structure of the chapter is as follows. First, it outlines some of the important events surrounding the thalidomide disaster in Sweden, identifying a number of key actors and events that preceded the foundation of the Register of Congenital Malformations. It contextualizes these events in relation to an international movement toward registries and control over pharmaceuticals. Second, it sketches a prehistory of the Register of Congenital Malformations and the main actors and debates leading up to its foundation, from the Tornblad Institute in Lund in southern Sweden, to the state inquiry into congenital malformation surveillance that was the forerunner to the register. Third, it delves into the practices of surveilling for unknown syndromes in a medical world obsessed with standardized paper technologies—and perhaps most importantly how the key actor, Bengt Källén, attempted to redesign the paper technologies of surveillance—to be able to sense the unknown in a world of knowns.

1 Thalidomide and the Emergence of Birth-Defect Surveillance

In the early 1960s thalidomide was found to cause grave birth defects.[6] The first signs of birth anomalies were discovered in West Germany, and the drug was recalled from the West German market in November 1961. However,

5 Bauer, 'From Administrative Infrastructure'; Bauer, 'Mining Data.'

6 Vargesson, 'Thalidomide-Induced Teratogenesis.'

thalidomide was still—even after the West German recall—sold on license outside Germany.[7] Nonetheless, owing to the mounting evidence of thalidomide's teratogenic effect on fetuses (i.e., that it causes congenital malformations), Swedish sales of the drug were halted a month later than in West Germany, on December 20, 1961.[8]

In the international medical literature, the first warning signals about thalidomide were sounded in the Lancet in 1961 and 1962 by William McBride and Widukind Lenz.[9] In Sweden, the Christian newspaper *Dagen* was the first to sound the public alarm in February 1962.[10] In March 1962, an article by A.-L. Bergström and coauthors, outlining the birth defects in Sweden, appeared in the Swedish medical journal *Svenska läkartidningen*.[11] Naturally, Swedish media headlines also reflected the fear of pharmaceutical damage to fetuses. For instance, in April 1962, a half page was devoted to the disaster. The page exclaimed, 'No pills—the fetus can be harmed!,' 'Fetal damage increased 300 times,' and 'Strong circumstantial evidence against thalidomide,' were published in the Swedish tabloid *Expressen*.[12] The fear of pharmaceutically induced malformations was palpable, and it contributed in many ways to the reshaping of how drugs were regulated, tested, and surveilled.[13]

Furthermore, in the wake of the thalidomide disaster, many countries set up registries for the reporting of birth defects. These were designed to be an early warning system for a new medically induced tragedy.[14] For instance, in Finland, a registry was founded in 1963.[15] In the United Kingdom a registry of malformations was set up in England and Wales in 1964.[16] In the United States,

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7 Lennerhed, 'Kvinnan, aborten och teratologin.'

8 Swedish Chancellor of Justice, Justitiekanslerns utlåtande angående neurosedynkatastrofen.

9 Lenz, 'Short History of Thalidomide Embryopathy'; Lenz et al., 'Thalidomide and Congenital Abnormalities'; Mcbride, 'Thalidomide and Congenital Abnormalities.'

10 Lennerhed, 'Kvinnan, aborten och teratologin.'

11 Bergström et al., 'Talidomid-embryopati.'

12 Bernholm, 'Fosterskador ökade 300 gånger,' 7.

13 In the wake of the thalidomide tragedy a number of changes to pharmaceutical testing and malformation surveillance were instituted, aimed at preventing and detecting another pharmaceutical disaster. One important change was the reshaping of how drugs were tested and regulated, leading many countries to institute mandatory reporting of pharmaceutical studies to regulatory bodies. The famous three-phase randomized controlled trial (RCT) was born. Vargesson, 'Thalidomide-Induced Teratogenesis'; Olszynko-Gryn et al., 'Historical Argument for Regulatory Failure.'

14 International Centre for Birth Defects et al., *World Atlas of Birth Defects*.

15 Finnish Institute for Health and Welfare, 'Medfödda missbildningar.'

16 Misra, 'Evaluation'; Misra, Dattani, and Majeed, 'Congenital Anomaly Surveillance.'

the Center for Disease Control first started surveilling birth defects in 1967.[17] In Norway, the Medical Birth Registry was founded in 1967.[18] Consequently, the institution of Sweden's Register of Congenital Malformations in 1964 was part of an international movement to curtail pharmaceutical disaster by surveilling birth defects. The thalidomide tragedy thus left a lasting impression on the institutionalization of pharmaceutical safety procedures and the surveillance of birth defects.

2 The Welfare State and the Registration of the Population

However, the institutionalization of the Register of Congenital Malformations was not solely a reaction to the thalidomide tragedy. It was also situated in a period when the medical and epidemiological registration of the population in the Nordic countries boomed.[19] During this period many other registries were established across the region.[20] In Sweden, the Twin Register was established at the end of the 1950s, and the Patient Register was created in 1964.[21] As a part of this development, the reporting of deaths in Sweden was centralized to the Statistical Bureau in 1951.[22]

Thus, the development of the Register of Congenital Malformations can be understood in the context of 'long traditions of social engineering [… and] politics that became associated with the "Scandinavian" welfare states' as well as the establishment and growth of register-based research and epidemiology in the Nordic countries and elsewhere. Susanne Bauer has argued that this mode of medical investigation has been key in the rise of a specific 'Nordic style' of epidemiology based on the constant collection of data about the population, where personal identification numbers also became important.[23]

In sum, the Register of Congenital Malformations was part of an international movement toward surveillance of birth defects following the thalidomide disaster, participated in a long Nordic tradition of registering the

17 Edmonds et al., 'Congenital Malformations Surveillance.'
18 Bjerkedal, 'Protection of Privacy.'
19 This tradition of registering statistics about the population dates back to the 1700s in Sweden. See also Bondestam's chapter in this volume.
20 Bauer, 'From Administrative Infrastructure.'
21 Lichtenstein et al., 'Swedish Twin Registry'; National Board of Health and Welfare. 'Historik om patientregistret.'
22 Johansson, *Dödsorsaksstatistik*.
23 Bauer, 'From Administrative Infrastructure.'

population, and contributed to an international push to standardize the classification of disease. Consequently, the foundation of the register can be situated in a broader shift toward what David Armstrong has dubbed 'surveillance medicine,' in which population-based studies were used to delineate the normal standard of, for instance, children's development, as well as to define abnormalities and identify risk factors in individuals.[24]

3 The Prehistory: Comparative Embryology, Bengt Källén, and the Tornblad Institute

The surveillance of congenital malformations in Sweden was intimately intertwined with the work of embryologist and epidemiologist Bengt Källén. Through his work, Källén would develop into the most important actor for the surveillance of congenital malformations in Sweden. Källén was to become long-time director of the Tornblad Institute in Lund, where the Register of Congenital Malformations was eventually located. He was also instrumental in the work leading up to the foundation of the register as well as sometimes its sole custodian.[25]

The Tornblad Institute was founded by the anatomy professor Ivar Broman as an institute of comparative embryology in 1934. Broman was an avid collector of embryos and fetuses, and the macabre jars of fetuses were until recently available at the institute.[26] In the early 1950s Källén wrote his dissertation on comparative embryology at the Tornblad Institute, which led him to take an early interest in the abnormalities of fetal developments.[27] He would later describe the register as linked to his previous work on comparative embryology as well as his interest in fetal abnormalities and 'monsters.'[28]

Thus, in the early 1960s, when the thalidomide disaster became apparent, Källén and the Tornblad Institute seemed well positioned for taking up the teratogenic challenge that had been laid down by McBride and Lenz—and in the Swedish context by Bergström and coauthors—when they sounded the alarm about thalidomide in 1961 and 1962 in the Lancet.

24 Armstrong, 'Rise of Surveillance Medicine'; Rose, 'Psychological Complex.'
25 Källén, *Tornblad Institute in Lund*, chap. 7.
26 Källén, *Tornblad Institute in Lund*; Jülich, 'Historier kring Tornbladinstitutet.'
27 Källén, *Tornblad Institute in Lund*, chap. 7.
28 Källén, *Tornblad Institute in Lund*, chap. 1.

4 The Teratogenic Effect of Drugs and the Foundation of the Register of Congenital Malformations

Before the Register of Congenital Malformations was founded, malformations had been collated, reported, and analyzed annually in Sweden.[29] In the wake of the thalidomide disaster this approach was increasingly understood to be unsatisfactory as an early warning system for drug-induced medical disasters. For instance, Bergström and coauthors suggested, in their article on thalidomide embryopathy from March 1962, that 'a continuous, central registration and analysis of certain malformations' could become an important means of understanding the causes of malformations.[30]

During the spring of 1962 surveillance of malformations and drug consumption commenced on a trial basis. On February 26, 1962, the Register of Congenital Malformations instructed all maternity wards to send in monthly reports, between March 1 and May 31, of any congenital malformations as well as all mothers' consumption of sleeping aids during the first half of pregnancy. These monthly reports led to the discovery of widespread consumption of sleeping aids on the part of the pregnant women. On May 29 the board instructed the maternity wards to continue reporting any congenital malformations, as well as the drug consumption of mothers with malformed infants. They thus narrowed the scope of reporting for drug consumption, from all mothers to only those who had given birth to malformed infants.[31] The board deemed surveillance to be of importance, but the exact methods were still being worked out.

In addition, on April 1, 1962, the National Board of Medicine decided to start an inquiry into the teratogenic effect of drugs. The board gave pediatrician Jan Winberg—who was also one of Bergström's coauthors on the March 1962 article that sounded the alarm about thalidomide in the journal *Svenska läkartidningen*—the task of investigating.[32] Winberg's inquiry was dubbed Utredningen angående sambandet mellan läkemedel och fosterskador (the Inquiry into the Relationship between Pharmaceuticals and Congenital Malformations). Its remit was broader than thalidomide, and aimed to openly investigate any links between drugs and congenital malformations.

In 1963, the sore of thalidomide was still raw, and owing to findings in Winberg's ongoing inquiry, two other drugs, Postafen and Postadoxin (based

29 Källén and Winberg, 'Erfarenheter av kontinuerlig registrering,' 1943–44.

30 Bergström et al., 'Talidomid-embryopati,' 1021.

31 Winberg, 'Utredning: IV.'

32 Swedish Chancellor of Justice, Justitiekanslerns utlåtande angående neurosedynkatastrofen.

on the compound meclizine), received a warning label from the National Board of Medicine: 'not for pregnant women.' The Postafen warning label became a topic of debate between Winberg and Källén—who would both lay the groundwork for the Register of Congenital Malformations—in the journal *Svenska läkartidningen*. The point of contention was how to handle the preliminary results from Winberg's studies of the teratogenic effect of drugs. Winberg defended the application of the warning label on the basis of his preliminary investigation, while Källén argued that it was a premature, even incorrect decision, not based in the statistical evidence.[33] However, the use of statistics concerning abnormalities in medical regulation was not an easy task, and it was impossible for the National Board of Medicine to make any conclusive decisions about Postafen or Postadoxin on the basis of the Winberg study.[34]

Thus, at an early stage, the challenges of bringing unruly bodies and malformations under statistical surveillance were debated and acknowledged by two of the most important actors in the surveillance of congenital malformations in Sweden, Källén and Winberg. Questions about drawing conclusions from uncertain medical statistics would follow Källén throughout his career, and he would become a prolific writer about the pitfalls and methodologies of statistical epidemiology. However, both Källén and Winberg's early work on congenital malformations would help pave the way for a central register of congenital malformations.

The report from Winberg's inquiry was eventually published in five parts in *Svenska läkartidningen* in 1964. In it he lamented the state of the yearly reporting of malformations, and he identified multiple challenges with this approach to the statistical surveillance of malformation—for instance, uncertain and imprecise classifications according to the *International Classification of Diseases*, as well as overreporting of very common and 'meaningless' malformations. Just as in the 1962 article that he coauthored with Bergström, he argued that 'the current form of reporting and registration of malformations is unsatisfactory.'[35]

Before Winberg's inquiry concluded, the National Board of Medicine decided to explore the feasibility of the national monthly registration of congenital malformations starting in April 1964.[36] The board gave the task of running the trial to Källén and Winberg; it entailed mandatory reporting

33 Källén, Sjövall, and Ursing, 'Läkemedel och fosterskador—en replik.'

34 Winberg, 'Utredning: v.'

35 Winberg, 'Utredning: i & ii'; Winberg, 'Utredning: iii'; Winberg, 'Utredning: iv'; Winberg, 'Utredning: v.'

36 Lennerhed, 'Kvinnan, aborten och teratologin'; Källén, *Tornblad Institute in Lund*.

from women's clinics and maternity wards that had a pediatric consultant.[37] In January 1965 this new form of registration was made permanent, and the Register of Congenital Malformations was born, requiring 60 percent of Sweden's births to be reported.[38] Hopes for the new registry were high, and Källén, its first head, argued that the thalidomide tragedy would have been detected in only five months if this new type of reporting and statistical surveillance had been in effect.[39]

5 Classifying Malformations at the Bedside: Unruly Bodies, Unruly Professionals

Before the Register of Congenital Malformations was instituted, the foundation for the statistical classification of birth defects was the well-known *International Statistical Classification of Diseases, Injuries and Causes of Death* (ICD). The ICD was, and still is, the internationally accepted standard for classifying disease, and was used for statistical purposes. In Sweden during this time, two versions of the ICD were in use in medical classification. Both were based on the seventh version of the ICD, which was ratified by the World Health Organization in Geneva in 1955. The first Swedish version was printed in 1957, and the second in 1965.

In the Swedish ICD from 1957 congenital malformations are classified in chapter XIV. The classification spans two pages, from '750 *Monstra*'[40] to unspecified malformations that are not classified elsewhere: '759 *Maleformationes congenitae aliae s. Non definitae, alibi non classificatae*.' The newer version of the ICD broke down the categories of malformations further, specifying each in more detail. For example, the old category 750 *Monstra* is divided into several new ones: '750,00 *Acrania*,' '750,10 *Monstrum* (*of duplex type*),' '750,20 *Monstrum* (of undeveloped body shape—usually of the type where the head transitions directly to the trunk),' '750,99 *Monstrum aliud et* UNS' (where 'UNS' stands for unspecified). The monsters of the early modern period are thus subdivided, and other categories are developed to bring the abnormal infant into statistical and medical nomenclature.[41]

37 Källén, *Tornblad Institute in Lund*, chap. 7.

38 Källén and Winberg, 'Erfarenheter av kontinuerlig registrering av missbildningar,' 1943–44.

39 Källén and Winberg, 'Swedish Register of Congenital Malformations.'

40 Which includes 'Monstrum simplex: Acephalus, anencephalus, macrocephalus, etc. Monstrum duplex: Acardius, ischiopagus, thoracopagus, etc. Epignatus. Monstrum UNS.'

41 For monsters, see Bondestam's chapter in this volume.

However, the practices of producing medical statistics often have to contend with a multitude of practical challenges. Constant work is needed to produce medical and epidemiological statistics—and this work is not only of mathematical or statistical nature.[42] Birth defect registration grappled with a multitude of unruly bodies and professionals. A constant stream of local practices were translated into records, statistics—hopefully giving a clear sign when something is amiss—the goal being to avert a new thalidomide disaster.

To open up a window into the unruly realities of birth defect surveillance, the archive from Winberg's inquiry provides unique insights into the practical realities of the making of medical statistics in hospitals. This archive comprises thirty-six boxes of material, of which sixteen contain copies of medical records from births of children with congenital malformations. The medical records are drawn from all over the country and stem from small rural hospitals to large central university hospitals. They document the childbirth itself, as well as descriptions of the infants with congenital malformations and their treatment. The records provide rich details concerning how physicians struggled to bring the abnormal under standardized control in the late 1950s and early 1960s.[43]

The medical records were written on standardized forms, which are mostly unique for each hospital, printed at the local printers, or in some cases bought from a central printer, such as the large Swedish office supply depot ESSELTE. The records range from short handwritten and mostly illegible forms documenting a birth and some type of malformation, to meticulously typed and documented case histories spanning twenty or more pages, including charts for temperature, weight, Rh factor, and infant feeding as well as statements from specialists in radiology, urology, or endocrinology. In some hospitals the records were stamped with '*Partus Normalis* 660a' or a scribbled note on the record which says 'Y20,0' both of which are ICD codes for normal childbirth.

The malformations documented in the records range from genital abnormalities to hip subluxations (instabilities of the hip) and everything in between. Latin and Swedish diagnoses are both used to describe the infants: *Micrognathia*, *Syndactylia*, *Sista benigna, Medfödd näsanomali*. At the larger hospitals, and sometimes at the smaller ones, ICD codes are added to the diagnoses: *Monstrum* with the ICD code Y38,6; *Melfarmatio crane* Y20,0 (deformed infant and normal birth); *Hydrocephalus* 752 Y38,7 (giving two different ICD codes for hydrocephalus); *Mongolismus* 759.3 (mongoloid with an ICD code in another category); *Syndaktilia pedis dx* 759.1 (ICD for *Maleformationes cutis*); *Luxatio cong*. 758.0

42 Bowker and Star, *Sorting Things Out*.

43 Records of Winberg's inquiry are available at NBM-AB.

(in the same ICD category); *Klumpfot* 758,6 (ICD for Other skeletal and joint malformations); and so on. Different versions of ICD codes are used, as are different languages. The 'Other' category is used with some frequency.

Sometimes the diagnosis is discussed in the record. The case histories can range from a couple of terse sentences to long accounts spanning several years of treatment. For example, in one record from Karlskoga Hospital, the infant is described in an emotional register: 'The child has miserable congenital malformations, partly ugly clubfeet, partly similar malformations in the wrists and partly very stiff joints in general.'[44] The language of the record betrays the physician's feelings toward the newborn child in terms of their 'miserable,' 'ugly,' and 'stiff' state—without commenting on the ICD code. Another record, from the Women's Clinic of Malmö Municipal Hospital, uses clinical language to describe and diagnose the infant, and notes the ICD codes of the diagnosis: 'A cyst-like growth under the tongue. Ref. to ear clin. Diagnosis: *Cysta sublinqnisinales* 759,3.'[45]

The variations in the material point to the monumental task of standardizing medical information: different hospitals, different physicians, different secretaries, and different affinities with the codes of the ICD. Each record reflects the knowledge, practices, and different levels of commitment to standardizing medical knowledge at a particular hospital. The work of creating statistical medical knowledge thus starts at the patient's bedside—and reflects different local commitments to standardized medical knowledge and the statistics of fetal malformations.

Furthermore, the unruliness of diagnosing infant bodies is brought out time and time again in the records. Jotted annotations, question marks in the margins of the diagnosis, and uncertain and interpretative language constantly appear. The uncertainty of diagnosing congenital abnormalities is vividly reflected. For example, the struggle to know whether a child is born with congenital hip subluxations is tied to interpreting X-ray images, as well as keeping an infant still at the moment of exposure:

> with outstretched and inwardly rotated legs you can possibly get an impression of the left femur being slightly lower laterally than the right. One of the images unfortunately not completely [unreadable] as the child moved at the moment of exposure. There is no certain basis for congenital hip dislocation, but cannot be ruled out either.[46]

44 Record from Karlskoga Hospital.
45 Record from Women's Clinic of Malmö.
46 Follow-up assessment record.

Here, the bodily and material realities of the diagnosis of infants, as well as the difficulty of determining the normal range of the infant's form are brought to the fore. What is the normal configuration of an infant body? What could be said to be a normal configuration of the infant's hips? Physicians struggled to make diagnoses and pin down the heterogeneity of the human body. Another example concerns hip dislocations: 'Definite signs of dislocation do not exist, but a certain suspicion does exist that the l. femur is both pushed up and laterally dislocated.'[47] The language of these records reflects the constant efforts of medical staff and the difficulty of pinning down the human body on the diagnostic grid of the ICD. Physicians brandished the language of uncertainty: 'possibly,' 'relatively,' 'suspicion,' 'uncertain,' 'impression,' 'cannot be ruled out.'

What we can discern in these records is the difficult work of standardizing abnormality in practice. First, the classification of malformations relates to a multiplicity of infrastructures: partly the local standards that are articulated in the preprinted medical forms, partly the different translations of the ICD-7 in use in Sweden at the time. Second, the records reveal different traces of the practices of classification: the difficulty of making a certain diagnosis at the bedside, different commitments to the nationwide standardized statistical classification, but also the strong tendency toward normalizing mothers and infants. Each localized practice leaving traces in the forms, notes, language, and classifications.

The next step in the statistical surveillance of congenital malformations was to coerce these multiplicities into a statistical norm for malformations. This brings us to the practices of producing a constant statistical surveillance of congenital malformations. How did Källén intend to detect and stop the next thalidomide disaster using the Register of Congenital Malformations?

6 Surveilling Unruly Malformations: Problems in Practice

Transforming the multiplicities of congenital malformations into statistical surveillance was, and still is, a monumental challenge. How do you bring the abnormal under statistical control? Källén, as outlined above, was a driving force for this surveillance effort in Sweden. He published numerous texts on the classification of malformations. And he worked tirelessly to use the unruly medical data to produce statistics. The challenges that Källén identified in surveilling congenital malformations were many.

47 Record from the Central Hospital in Kalmar, Maternity Ward.

One challenge was that the very definition of malformation is multifarious and indefinite. Källén describes the border between an 'anatomical variation' and a malformation as uncertain, which in turn affects how classification is done in practice. Different research materials define the same diagnoses differently. Some are treated as a malformation, while others are not:

> The definition of malformation is fluid. The boundary against anatomical variations is often uncertain. Some materials have included anatomical variations, that are excluded in other materials. This often pertains to comparatively insignificant defects with relatively high frequency, which can completely skew the statistics. A clear definition of what has been registered as a malformation in a specific study is required, if the frequency numbers are to have any value.[48]

The challenge that Källén identifies thus points back to the practices of classification in different studies. His argument is that the interpretation of what a malformation is in local practices, and in specific investigations, will create completely different statistical understandings of malformations. In an interview in which Källén reflected on the early years of the Register of Congenital Malformations, he discussed the impossibility of classifying malformations using the grid defined in the ICD. The range of variation in congenital malformations constantly broke the standardized reporting formats of the ICD. The classes and diagnoses of the ICD were much too coarse to be useful for capturing the multifariousness and variability of medical malformations.[49]

Källén also ties the problem of standardized reporting of malformations to diagnostic practices and technologies, as well as the professional training and role of the diagnosing physician. In a textbook on teratology from 1967 he reflects on how classification procedures and practices vary:

> The diagnosis of a malformation can vary in exactness between different investigators. […] In standardized reporting there is a larger risk that malformations are omitted. Experience shows that even easily observed malformations, for example cleft lip and grave defects of extremities are underreported. The precision of the diagnosis will also be dependent on whether autopsy is performed, if different exams (e.g. X-ray) have been performed, and whether the exam is performed by a pediatrician or pathologist or by nonspecialist physicians, midwives etc.[50]

48 Källén, *Teratologi*, 31.
49 Källén, interview with the author.
50 Källén, *Teratologi*, 31.

Here Källén gets close to how bedside practices reshape medical statistics and medical data. He brings up how easily observed malformations are not reported, and how certain malformations are not observable without specific forms of infrastructure and examination, such as X-rays. He also mentions that the training and experience of different professional groups skew statistics. In sum, he ties the statistical surveillance of congenital malformations to the varying classification practices of bedside reporting.

A further challenge that Källén brings up, in relation to reducing the explosive growth of medical archives in Sweden, is the impossibility of summarizing records without foreclosing the possibility of historical studies of congenital malformations. For instance, in a journal article he argues against archival deselection or even summarizing medical records to save space, since the knowledge and interests of the diagnosing physician will shape what the summary will contain, precluding future investigators from reclassifying the material:

> It is clear that the continued growth of the record archives must be slowed. Many different technical solutions can be discussed. An imminent possibility is to create record summaries, which are archived, while the record itself is destroyed after an appropriate time. Of course, such a record summary can also be stored in appropriate memory, e.g. a database. I would strongly advise against this possibility. The summary will reflect the summarizing person's knowledge and interests—it is impossible to predict what will be interesting in the future. […] When writing the summary, some information is suppressed, which the summarizing physician deems to be uninteresting, leading to a nonrandom selection.[51]

The problem of summarizing medical records, according to Källén, is again tied to the practices of medical classification. Any summarizing of information will, according to Källén, reflect the current knowledge and interests of the person that summarizes the information. He also points to the impossibility of knowing what information could become interesting in the future. According to Källén, the original record—the messy, unruly documentation of the diagnosing medical personnel—needs to be retained in order to surveil congenital malformations. He ties this challenge back to the thalidomide tragedy, and how yearly summaries of birth defects were not sufficient to identify the relevant malformations among other more common ones:

51 Källén, 'Medicinsk-genetiska synpunkter på journalgallring,' 33.

> A concrete example of this is that, when the thalidomide injuries in neonates began to occur, it was not possible to distinguish these extremely specific and previously exceptionally unusual injuries from a number of other and common malformations of the extremities that were not related to thalidomide in the current summaries (annual reports).[52]

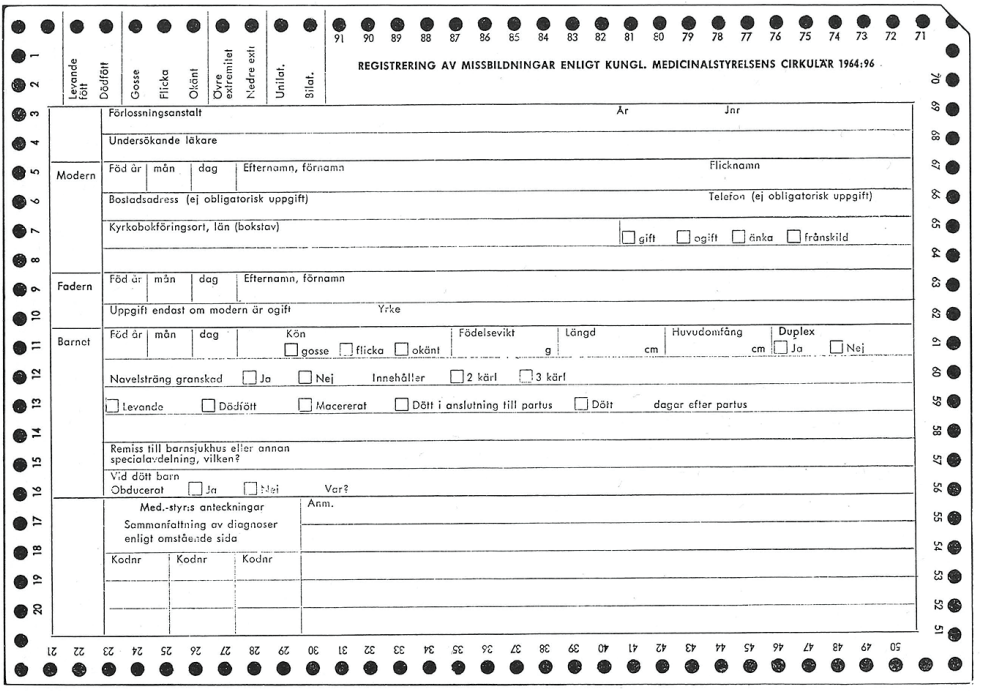
Again, Källén emphasized how the knowledge and interests of the person making the summary were not targeted enough to be able to perceive the change in statistical malformation patterns during the thalidomide disaster. The specific forms of malformations that the thalidomide disaster created were not possible to discern from the usual pattern of malformations. The existing standardized statistical classifications were not precise enough to be able to see the unexpected new patterns of malformation that emerged after the thalidomide disaster.

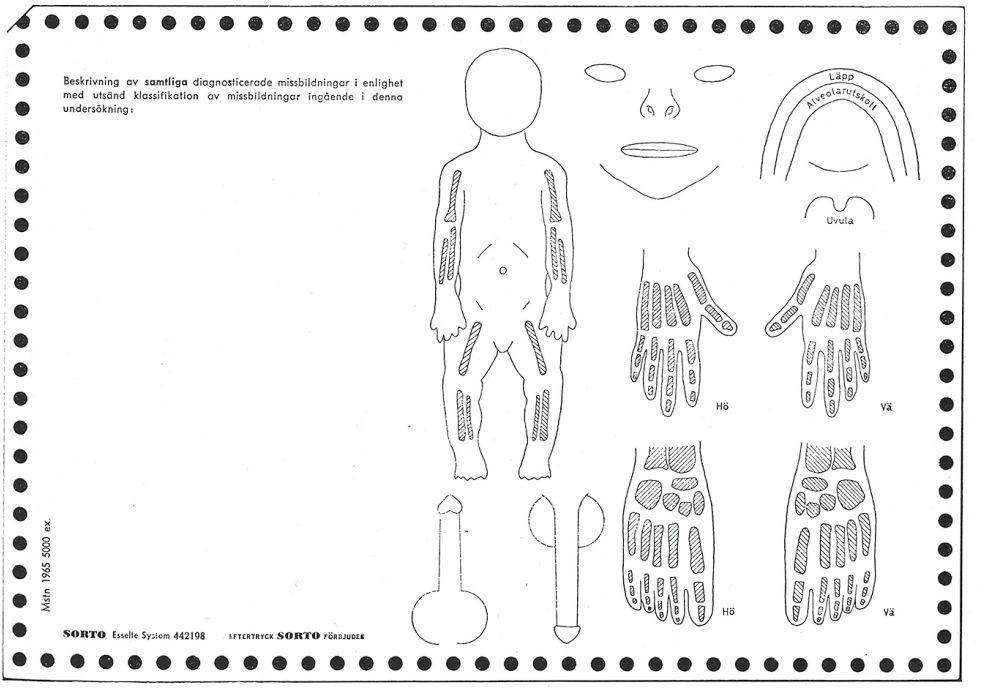
7 The Material Practices of Congenital Surveillance: Breaking Free from the ICD

In his constant attempts to solve the challenges of the surveillance of congenital malformations, Källén developed several methods for dealing with unruly and unclassifiable abnormalities, and the varying knowledge of the diagnosing personnel. For Källén the transformation of malformations into surveillance was a sustained effort. He struggled tirelessly to surveil congenital malformations as he attempted to create and run an early warning system that would protect against another thalidomide tragedy.

One attempt to solve the matter of imprecise reporting was specifically designed reporting cards that the National Board of Medicine distributed to all hospitals in Sweden. Information about congenital malformations was supposed to be recorded on these cards at the bedside of the patient. The cards showed a diagram of an infant, on which the physician was instructed to mark the location of the malformation on the back of the card, and to describe it verbally as clearly as possible. These reporting cards were then to be sent to the Register of Congenital Malformations, to be coded for the purposes of statistical surveillance. The cards were printed on thick, stiff paper, to make it easier for physicians to jot down their diagnosis at the bedside. But according to Källén these forms were also intended to create friction for the medical secretaries

52 Källén, 'Medicinsk-genetiska synpunkter på journalgallring,' 33.





FIGURES 11.1 AND 11.2 Front and back of the report card designed by Bengt Källen. From Källén and Winberg, 'Register of Congenital Malformations,' 765–76.

who often typed the diagnoses on the forms. The stiff cards were purposefully difficult to get into the typewriter. By employing the cards' materiality, Källén wanted to entice hospital workers to collect the information directly from the source, while local physicians sometimes preferred to delegate the reporting work to a medical secretary.[53]

By requiring the reports to conform to this system, Källén hoped to bypass the coarse grid of the ICD diagnosis, as well as the shaping influence of the interests and knowledge of the diagnosing physicians. The report card purposefully asked for a bodily location and description of the malformation. Källén's hope was that his system would allow the reporting of *unknown* anomalies—the abnormalities that did not fit into the established grid of medical diagnosis. By doing this he attempted to keep alive the unruliness of congenital malformations, and allow for the unknown and unruly to be reported.

However, regardless of the reporting cards, Källén faced the same challenge as the diagnosing physicians: to categorize and classify the malformations for statistical analysis. What is a normal bodily malformation? What is the same malformation? What is a new abnormality? What is an unknown anomaly—perhaps caused by a new teratogenic pharmaceutical?

To classify the constant stream of reporting cards Källén argued that the crude grid of the ICD was not enough. Källén therefore created his own bespoke coding scheme, which was adapted to the latest data-processing technologies. He argued that the advantage of his system was the flexibility that it afforded in adding categories, when new malformations were discovered—for each newly discovered malformation, Källén himself could create a new category.[54]

The person translating the constant stream of report cards into statistical codes was Källén himself. He traveled regularly from his workplace in Lund, in the south of Sweden, to the National Board of Medicine in Stockholm to harvest new report cards, classify them, and enter them into the statistical analysis. By organizing the statistical classification of malformations in this manner, Källén attempted to address the many and difficult challenges that he had identified in surveilling congenital malformations. Using the report cards and his own code list, Källén attempted to solve several problems of standardizing the abnormal: he retained some of the unruliness of the bodily descriptions in the report cards, not immediately discarding description for classification; he attempted to make a finer grid of classifications in his own code list, circumventing the coarseness and inflexibility of the ICD; and by carrying out the coding alone, he tried to reduce the variations that resulted from

53 Källén, interview with the author.

54 Källén, interview with the author.

1XXXX missbildning i CNS	*CNS malformation*
11XXX slutningsmissbildning CNS	neural tube defect
11100 anencefali (akrani)	anencephaly
11210 myelomeningocele anterior	anterior MMC
11220 myelomeningocele posterior	spina bifida aperta
11300 encephalocele	encephalocele
11400 spina bifida utan myelomeningocele	spina bifida without MMC
11500 dermal sinus motsvarande spina bifida	dermal sinus at spina bifida
11600 defectus capilliti eller ländrygg	defectus capilliti or lumbar
12000 mikrocefali	microcephaly
13000 hydrocefali	hydrocephaly
14100 hydranencefali	hydranencephaly
14200 porencephali, hjärncystor	porencephaly, cerebral cysts
15000 holoprosencephali, arrhinencefali	holoprosencephaly
16XXX övriga CNS-missbildningar	other CNS malformations
16100 Möbius syndrom	Moebius syndrome
16110 centronukleär myopati	centronuclear myopathy
16210 cerebellär hypoplasi	cerebellar hypoplasia
16220 övrig cerebellär missbildning	other cerebellar malformation
16310 pakygyri i cerebrala cortex	pakygyria of cerebral cortex
16320 mikropolygyri i cerebrala cortex	micropolygyria, cerebral cortex
16330 övrig missbildning i cerebrala cortex	other cerebral cortex malform.
16400 agenesi av corpus callosum	agenesis of corpus callosum
16401 AV fistel corpus callosum	AV fistula in corpus callosum
16402 dysgenesi av corpus callosum	dysgenesis of corpus callosum
1650x facialispares	facial paresis
16600 diastematomyeli	diastematomyelia
16700 makrocefali	macrocephaly
16800 cebocefali (=15000)	cebocephaly (=15000)
16900 diverse hjärnmissbildningar	other brain malformations
16901 Dandy Walker cysta	Dandy Walker cyst
16902 aplasi av occipitalloben	occipital lobe aplasia
16990 oklar ryggmärgsmissbildning	unclear spinal cord malform.
16991 del av ryggmärg saknas	part of spinal cord missing
2XXXX missbildningar i sinnesorgan	*sensory organ malformations*
21XXX ögonmissbildningar	*eye malformations*
21100 cyklopi	cyclopia
21101 pseudocyklopi (tättsittande ögon)	pseudocyclopia
2121x anoftalmi	anophthalmia
2122x mikroftalmi	microphthalmia
2123x kryptoftalmi	cryptophthalmia
213XX slutningsdefekter av ögonen	eye closure defect
21311 iriscolobom	coloboma of iris
21312 retinacolobom	coloboma of retina
21313 linscolobom (=2151X)	coloboma of lens (=2151X)
21314 komplicerat colobom	complicated coloboma
21315 excentrisk pupill	excentric pupilla
21316 colobom av palpebrae	coloboma of eye lid
2132x mikroftalmi med cysta	microphthalmia with cyst
2140x aniridi	aniridia
2151x coloboma lentis	coloboma lentis
2152x afaki	aphakia
2153x linsektopi	lens ectopia

FIGURE 11.3 A page from Bengt Källén's list of malformations. Courtesy of Bengt Källén

the different knowledges and interests of various professional groups.[55] It was Källén's know-how and experience that became the standard.

8 Statistical Surveillance and the Challenge of the Unknown

Medical statistics concerning malformations in the 1960s as well as today are based on unruly practices of classification and standardization of bodies that constantly break our grids of understanding. In statistical disease surveillance, the properties of any new disease are unknown—it is impossible to know what to be on the lookout for. What are the symptoms of a new thalidomide tragedy? What is a warning signal that a new pandemic flu has emerged? How do we know whether a new hemorrhagic fever is making its first cases known? In patient records—in the unruly diagnostic practices of different physicians, hospitals, or professions—might lurk the unknown disaster or disease.

In one publication, Källén argued that he would have been able to detect the thalidomide tragedy statistically only five months after its first cases were reported.[56] But that argument was of course made in hindsight, when the symptoms of the syndrome were already well known. He knew what to look for, and could therefore group the familiar malformations together in a recognized configuration.

In grappling with these challenges at the Register of Congenital Malformations, Källén devised a number of devices to help him detect, delineate, and act on new and unknown diseases. First, the reporting cards, where he attempted to entice medical personnel to report on symptoms and observed defects rather than ready-made diagnoses. Second, his bespoke and potentially infinite list of classifications was made to accommodate any new malformations. Both these tools put Källén's knowledge and experience at the center of the surveillance of congenital malformations. He thus attempted to make himself the central hub for detecting any new unknown disease. If a new malformation started to rear its head, Källén, using the report cards and his own list of malformation codes, hoped to be able to discern this new development through statistical comparison.

What Källén did in the setup of the Register of Congenital Malformations was to organize the classification and counting of malformations in a center of calculation, thus attempting to control how malformations were classified and

55 Källén, interview with the author.

56 Källén and Winberg, 'Swedish Register of Congenital Malformations.'

counted in the statistical surveillance.[57] However, the reporting of the cases and the filling in of the forms—and thus the first decision to count a specific biological variation as a malformation—were still delegated to the local hospitals. These decisions, sometimes made at the bedside by the reporting physician, and sometimes by medical secretaries, remained outside Källén's control, creating challenges in terms of the validity of the statistical inferences.

9 Sketching the History of the Register of Congenital Malformations

This chapter has sketched the history and material practices of birth defect surveillance in Sweden in the late 1950s and early 1960s. In doing this, it has first outlined the history, actors, and institutional work involved in setting up the Register of Congenital Malformations. It has situated the register in an international context, at the advent of medical regulation and surveillance, linking this development to the emergence of a Nordic style of epidemiology, based in the registration of the population.[58] Second, the chapter delves into the challenges and material practices of birth defect surveillance, especially those that abnormalities pose for medical-statistical surveillance. In this, it outlines how the unruliness of congenital malformations leads to a number of material practices that attempt to make them amenable to statistical surveillance.

In tracing the history of the Register of Congenital Malformations, this chapter brings to the fore certain challenges involved in the production of standardized medical knowledge. It highlights the difficulty of classifying congenital malformations in practice, the problems that arise in handling congenital malformations through standardized means, such as the ICD, and the struggles of medical practitioners to fit congenital malformations into the existing grid of medical classification. The multiplicity of congenital malformations constantly breaks out of the boundaries of medical standardization.

But perhaps more importantly, the chapter also brings to light the tensions between the unknown emerging syndrome and the known and standardized diagnosis in the surveillance of congenital malformations—and perhaps in medical surveillance for the unknown more broadly. According to Källén, the sensing infrastructure of medicine was steeped in physicians' judgment and previous knowledge as well as in the historically sedimented codes of the ICD—making it difficult to make room for and detect the unknown and emerging syndrome. This state of affairs spurred Källén to

57 Latour, *Science in Action*.

58 Bauer, 'From Administrative Infrastructure.'

centralize classification and judgment to his office—creating a center of classification and calculation—and to invent a bespoke and seemingly infinitely customizable classification system to break out of the sedimented and ready-made knowledge infrastructures of the medical system. His purpose was to invent an infrastructure for registry-based statistical surveillance—to make it possible to detect the unknown. In a sense he was trying to break away from—he resisted and reinvented—the existing paper technologies of classification (the ICD and preprinted diagnostic forms). He made his own bespoke paper-based infrastructure, attempting to remove physicians' judgments from the edges of this network, to form a controlled, one-man center of classification and calculation.[59]

One lesson here is about the tension between surveillance infrastructures—paper technologies of medicine—and the unruly and unknown syndrome. The chapter exemplifies how classification infrastructures and practices simplify, hide, split apart, or sometimes even do violence to the things they classify.[60] However, another lesson is about the tension between the already-known and classified and the emerging and unknown in surveillance medicine; it points to the infrastructural tensions between the ready-made and the bespoke, between the sedimented and the floating, and between nosology and unknown syndromes. The paper technologies of medicine create well-worn paths of classification that are difficult to break out of.

Bibliography

Armstrong, David. 'The Rise of Surveillance Medicine.' *Sociology of Health & Illness* 17, no. 3 (June 1, 1995): 393–404.

Bauer, Susanne. 'From Administrative Infrastructure to Biomedical Resource: Danish Population Registries, the "Scandinavian Laboratory," and the "Epidemiologist's Dream."' *Science in Context* 27, no. 2 (June 2014): 187–213.

Bauer, Susanne. 'Mining Data, Gathering Variables and Recombining Information: The Flexible Architecture of Epidemiological Studies.' *Studies in History and Philosophy of Science Part C: Studies in History and Philosophy of Biological and Biomedical Sciences* 39, no. 4 (December 2008): 415–28.

Bergström, A.-L., L. Nilsson, B. Pettersson, L. Söderling, L. Victorin, and J. Winberg. 'Talidomid-embryopati.' *Svenska läkartidningen* 59, no. 13 (1962): 1012–22.

59 Hess and Mendelsohn, 'Case and Series'; Hess, 'Paper Machine'; Mak and Bultman, 'Identity in Forms.' On centers of calculation, see Latour, *Science in Action*.

60 Bowker and Star, *Sorting Things Out*.

Bernholm, Bernt. 'Fosterskador ökade 300 gånger: Starka indicier mot neurosedyn.' *Expressen*, April 30, 1962.

Bjerkedal, Tor. 'Protection of Privacy against Protection of Health.' *Acta Obstetricia et Gynecologica Scandinavica* 79, no. 6 (June 2000): 520–22.

Bowker, Geoffrey C., and Susan Leigh Star. *Sorting Things Out: Classification and Its Consequences*. Cambridge, MA: MIT Press, 1999.

Carachi, Robert, and Sameh Helmi Edward Doss, eds. *Clinical Embryology: An Atlas of Congenital Malformations*. Cham: Springer International, 2019.

Edmonds, Larry D., Peter M. Layde, Levy M. James, J. William Flynt, J. David Erickson, and P. Oakley Godfrey. 'Congenital Malformations Surveillance: Two American Systems.' *International Journal of Epidemiology* 10, no. 3 (1981): 247–52.

Finnish Institute for Health and Welfare. 'Medfödda missbildningar.' September 4, 2020. https://thl.fi/sv/web/thlfi-sv/statistik/information-om-statistiken/kvalitetsbeskrivningar/missbildningar.

Hess, Volker. 'A Paper Machine of Clinical Research in the Early Twentieth Century.' *Isis* 109, no. 3 (September 1, 2018): 473–93.

Hess, Volker, and J. Andrew Mendelsohn. 'Case and Series: Medical Knowledge and Paper Technology, 1600–1900.' *History of Science* 48, no. 3–4 (September 2010): 287–314.

International Centre for Birth Defects, EUROCAT, World Health Organization, and Human Genetics Programme. *World Atlas of Birth Defects*. Geneva: Human Genetics Programme, Management of Noncommunicable Diseases, World Health Organization, 2003.

Johansson, Lars Age. *Dödsorsaksstatistik: Historik, produktionsmetoder och tillförlitlighet*. Stockholm: Socialstyrelsen, 2010.

Jülich, Solveig. 'Historier kring Tornbladinstitutet.' In *Embryologiska rum: Tornbladinstitutets samling av foster från människor och djur*, by Malin Thomas Nilsson and Solveig Jülich, 151–268. Göteborg: Makadam, 2022.

Källén, Bengt. Interview with the author. October 2018.

Källén, Bengt. 'Medicinsk-genetiska synpunkter på journalgallring.' *Arkiv, Samhälle och Forskning*, no. 21 (1979): 29–33.

Källén, Bengt. *Teratologi: Läran om missbildningar*. Stockholm: Almqvist & Wiksell, 1967.

Källén, Bengt. *The Tornblad Institute in Lund: From Comparative Embryology to Reproduction Epidemiology*. Lund: Royal Physiographic Society of Lund, 2014.

Källén, Bengt, Alf Sjövall, and Ingrid Ursing. 'Läkemedel och fosterskador—en replik.' *Svenska läkartidningen* 60 (1963): 1700–1703.

Källén, Bengt, and Jan Winberg. 'Erfarenheter av kontinuerlig registrering av missbildningar.' *Läkartidningen* 63, no. 20 (1966): 1941–51.

Källén, Bengt, and Jan Winberg. 'A Swedish Register of Congenital Malformations: Experience with Continuous Registration during 2 Years with Special Reference to Multiple Malformations.' *Pediatrics* 41, no. 4 (1968): 765–76.

Latour, Bruno. *Science in Action*. Cambridge, MA: Harvard University Press, 1987.

Lennerhed, Lena. 'Kvinnan, aborten och teratologin.' *Lychnos* (2015): 141–63.

Lenz, Widukind. 'A Short History of Thalidomide Embryopathy.' *Teratology* 38, no. 3 (1988): 203–15.

Lenz, Widukind, R. A. Pfeiffer, W. Kosenow, and D. J. Hayman. 'Thalidomide and Congenital Abnormalities.' *Lancet* 279, no. 7219 (January 6, 1962): 45–46.

Lichtenstein, Paul, Patrick F. Sullivan, Sven Cnattingius, Margaret Gatz, Sofie Johansson, Eva Carlström, Camilla Björk, et al. 'The Swedish Twin Registry in the Third Millennium: An Update.' *Twin Research and Human Genetics* 9, no. 6 (December 1, 2006): 875–82.

Mak, Geertje, and Saskia Bultman. 'Identity in Forms: Paper Technologies in Dutch Anthropometric Practices around 1900.' *International Journal for History, Culture and Modernity* 7, no. 1 (November 2, 2019): 64–109.

Mcbride, William G. 'Thalidomide and Congenital Abnormalities.' *Lancet* 278, no. 7216 (December 16, 1961): 1358.

Misra, T. 'Evaluation of the National Congenital Anomaly System in England and Wales.' *Archives of Disease in Childhood—Fetal and Neonatal Edition* 90, no. 5 (September 1, 2005): F368–73.

Misra, T., N. Dattani, and A. Majeed. 'Congenital Anomaly Surveillance in England and Wales.' *Public Health* 120, no. 3 (March 1, 2006): 256–64.

National Board of Health and Welfare. 'Historik om patientregistret.' Socialstyrelsen, January 30, 2019. https://www.socialstyrelsen.se/statistik-och-data/register/alla-register/patientregistret/historik/.

Olszynko-Gryn, Jesse, Eira Bjørvik, Merle Weßel, Solveig Jülich, and Cyrille Jean. 'A Historical Argument for Regulatory Failure in the Case of Primodos and Other Hormone Pregnancy Tests.' *Reproductive Biomedicine & Society Online* 6 (August 2018): 34–44.

Rose, Nikolas. 'The Psychological Complex: Mental Measurement and Social Administration.' *Ideology & Consciousness* 5 (1979): 5–68.

Singh, Poonam Khetrapal. 'World Birth Defects Day: Many Birth Defects, One Voice.' Accessed 15 August, 2023. https://www.who.int/southeastasia/news/detail/02-03-2023-world-birth-defects-day-many-birth-defects-one-voice.

Swedish Chancellor of Justice. Justitiekanslerns utlåtande angående neurosedyn-katastrofen. Reg. no. 3195-02-90, April 30, 2003. https://www.jk.se/beslut-och-yttranden/2003/04/3195-02-90/.

Swedish Code of Statutes in the Field of Health and Sick Care. 'Kungliga Medicinalstyrelsens cirkulär angående rapportering av nyfödda med missbildning den

18 december 1964.' In *Samling av författningar och cirkulär m.m. angående medicinalväsendet*. MF 1964:96. Stockholm: Kungl. Medicinalstyrelsen, 1965.

Vargesson, Neil. 'Thalidomide-Induced Teratogenesis: History and Mechanisms.' *Birth Defects Research* 105, no. 2 (June 2015): 140–56.

Winberg, Jan. 'Utredning rörande det eventuella sambandet mellan fosterskador och läkemedel: Del I & II.' *Svenska läkartidningen* 61, no. 10 (1964): 718–41.

Winberg, Jan. 'Utredning rörande det eventuella sambandet mellan fosterskador och läkemedel: Del III.' *Svenska läkartidningen* 61, no. 11 (1964): 814–31.

Winberg, Jan. 'Utredning rörande det eventuella sambandet mellan fosterskador och läkemedel: Del IV.' *Svenska läkartidningen* 61, no. 12 (1964): 890–902.

Winberg, Jan. 'Utredning rörande det eventuella sambandet mellan fosterskador och läkemedel: Del V.' *Svenska läkartidningen* 61, no. 13 (1964): 980–87.

Archival Sources

Follow-up assessment record from the Maternity Ward at the Central Hospital in Kalmar, 1961, no. 281. Inquiry into the Relationship between Pharmaceuticals and Congenital Malformations. F54:1 (1962). NBM-AB.

Record from the Central Hospital in Kalmar, Maternity Ward, 1961, no. 215. Inquiry into the Relationship between Pharmaceuticals and Congenital Malformations. F54:1 (1962). NBM-AB.

Record from Karlskoga Hospital, no. 486/59. Inquiry into the Relationship between Pharmaceuticals and Congenital Malformations. F54:1 (1962). NBM-AB.

Record from Women's Clinic of Malmö Municipal Hospital, no. 2960/56. Inquiry into the Relationship between Pharmaceuticals and Congenital Malformations. F54:2 (1962). NBM-AB.