

Time trends of spina bifida in Sweden 1947–81

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SUMMARY The spina bifida rate in Sweden from 1947 to 1981 has been studied using various sources of information, including two central computerised registers. During the period the rate approximately halved, but the decline was not smooth and occurred in three “waves.” When the geographical location of high risk areas within each wave was studied, they were found to differ. The findings are discussed in the light of an environmental aetiology hypothesis of this malformation.

The reported prevalence of neural tube defects (NTD) varies by geographical location and over time. A classic study retrospectively showed an “epidemic” occurring in the Boston area with a peak prevalence at birth in 1930 and ending in about 1950.¹ Janerich described a continued decreasing rate in New York State from 1945 to 1971.² The continuing falling rate of NTD in the north eastern United States made Stein *et al* put the question: “Is myelomeningocele a disappearing disease?”³

Also, in other parts of the world, a decreasing rate of NTD has been described during the past few decades. In the 1981 annual report of the International Clearinghouse of Birth Defects Monitoring Systems (ICBDMS) a summary was given of data from 16 different monitoring systems round the world, but six could only supply data for a few years.⁴ A declining rate could be seen in England-Wales,⁵ N Ireland,⁶ Atlanta,⁷ and Hungary and Canada⁴—all areas with a comparatively high NTD rate around 1970. In some countries this rate is relatively low (10 or fewer in 10 000 births at the end of the 60s) and some further decline may be seen in some areas (Sweden, Finland, Denmark) but not in others (Norway, South America). A recent report from the Netherlands⁸ describes a pronounced decrease in anencephaly rate and declining trends were found also in New South Wales and Australia.⁹

In 1965 Sweden was a low prevalence area with a total NTD rate of about 1:1000, half of which were anencephaly and half were spina bifida. A continued decrease in rate occurred in the period 1965–81 as shown in the ICBDMs report.⁴ Our first question was: Is the low prevalence the end of a previous decline period from higher rates? We tried to answer this question by going back to 1947. The second question was: Are long term trends in NTD rates the

same in all parts of Sweden or are there local differences in changes of rates? We know of no other study which has combined time trend and geographical distribution patterns within one population. The presence of geographically different NTD rates in different parts of the world or within a country is, however, well known. A recent study describes this phenomenon in the United States.¹⁰ Well known high prevalence areas are located in Ireland, Scotland, and Wales (cf ref 11).

Material and methods

Two registers can give information on malformations in Sweden. One is the Register of Congenital Malformations (RCM) which has existed since 1965.¹² To this register—which before 1973 did not cover all Sweden—all infants with severe malformations (including NTD) should be reported. Reports are given in the form of verbal descriptions, not as codes, and contain reports on stillbirths and live births. Some underascertainment exists in the register. The prevalence figures included in the above mentioned ICBDMs report were based on this register. The second register is the Medical Birth Register (MBR) which contains the computerised summaries of all delivery records in the country since 1973, including malformation diagnoses, given as ICD codes. Both stillbirths and live births are included.

After 1973, information from both registers may be matched and in this way a reasonable—although not complete—ascertainment can be obtained, probably more than 90%. The two surveillance systems have been compared with respect to ascertainment and quality.

Before 1972, each delivery hospital in the country had to prepare a yearly report to be sent to the National Board of Health and Welfare (then "Medicinalstyrelsen") where these reports were stored. They give, among other things, number of births and perinatal mortality, and list malformed infants. Obviously, this source of information is not very reliable for minor malformations but was thought to be useful for severe malformations. For anencephaly, however, coding often occurred as "monster" or "multimaleformed baby," and it would be necessary to go back to individual records to sort out the true anencephalics. We therefore limited our study to cases of spina bifida, and all reports available for the period 1947–71 were read. The number of births for each hospital and the number of cases with spina bifida were recorded for each year. The set of yearly reports were not complete, reports from some hospitals were missing, but we hope that this was a random deficit. Obviously, only yearly reports that gave both the denominator (number of births) and the numerator (number of spina bifida) were included.

Results

Figure 1 shows the rates of spina bifida per 1000 births as determined from three sources: the yearly reports, the Register of Congenital Malformations, and the combined Register of Congenital Malformations and the Medical Birth Register. The

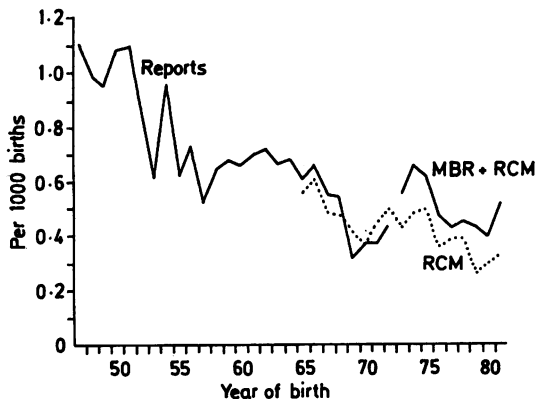


Fig 1 Registered prevalence at birth of spina bifida in Sweden, 1947–81. From 1947 to 1971 the graph is based on annual reports from the delivery hospitals (reports, —), from 1965 onwards also on reports to the Register of Congenital Malformations (RCM,), and from 1973 total registered rate in both RCM and the Medical Birth Register (MBR+RCM, whole graph) is marked.

*Each county is identified with a letter that is given in the table and in fig 3.

latter graph—which is available only from 1973—probably gives a reasonable estimate of the actual prevalence at birth of this malformation in Sweden and lies higher than the RCM graph. For the interval 1965–71, the RCM graph and the graph based on the yearly reports are relatively similar and these two systems probably have about the same rate of ascertainment. For 1972 the information from both the yearly reports and the Medical Birth Register is missing.

Figure 1 shows a pronounced decrease in registered rate between the late 1940s and middle 1950s, an increase to the middle 1960s followed by a decrease to about 1970. In the middle of the 1970s a slight increase occurred with a decline towards the end of that decade, followed by an indicated—but not certain—tendency to an increase in 1980–1.

This graph indicates that the spina bifida rate more than halved from the middle 1940s to about 1970. If spina bifida represents about half of the NTD cases this would mean that there was a general decline from perhaps 1:500 to less than 1:1000 during this period. This decline, however, occurred unevenly with at least three successive waves.

To study possible differences in time trends in different parts of Sweden, the expected and observed rates for each year were calculated for each county. The expected rates were then estimated from the rate in the whole country that year, based on data from the yearly reports and the Register of Congenital Malformations. For each county, a graph was prepared, showing the expected rates and the observed rates based on the same registers—the latter based on moving five yearly averages in order to reduce the effect of random fluctuations of low numbers. Figure 2 A–G shows examples of such graphs. The dashed sections of the county graphs indicate that there is no information found during that period.

Stockholme county (counties A+B,* fig 2) which contains the capital, Stockholm, consistently shows a somewhat lower than expected rate, especially pronounced in the beginning of the period and during the peak in the middle of the 1960s, whereas the rate in the middle of the 1970s is about the expected one. The Uppsala county (county C, fig 2 B) shows a lower than expected rate only in the peak of the middle of the 1960s, and this is true also for the Örebro county (county T, fig 2 G). In contrast to this, an extremely high rate is seen in Jönköping county (county F, fig 2 C) both in the first part of the period and during the peak in the middle of the 1960s, whereas Blekinge county (county K, fig 2 F) shows high rates also in the third peak in the middle of the 1970s. The Kristianstad county (county L, fig 2 E) shows a decline in rate between the end of the 1940s and

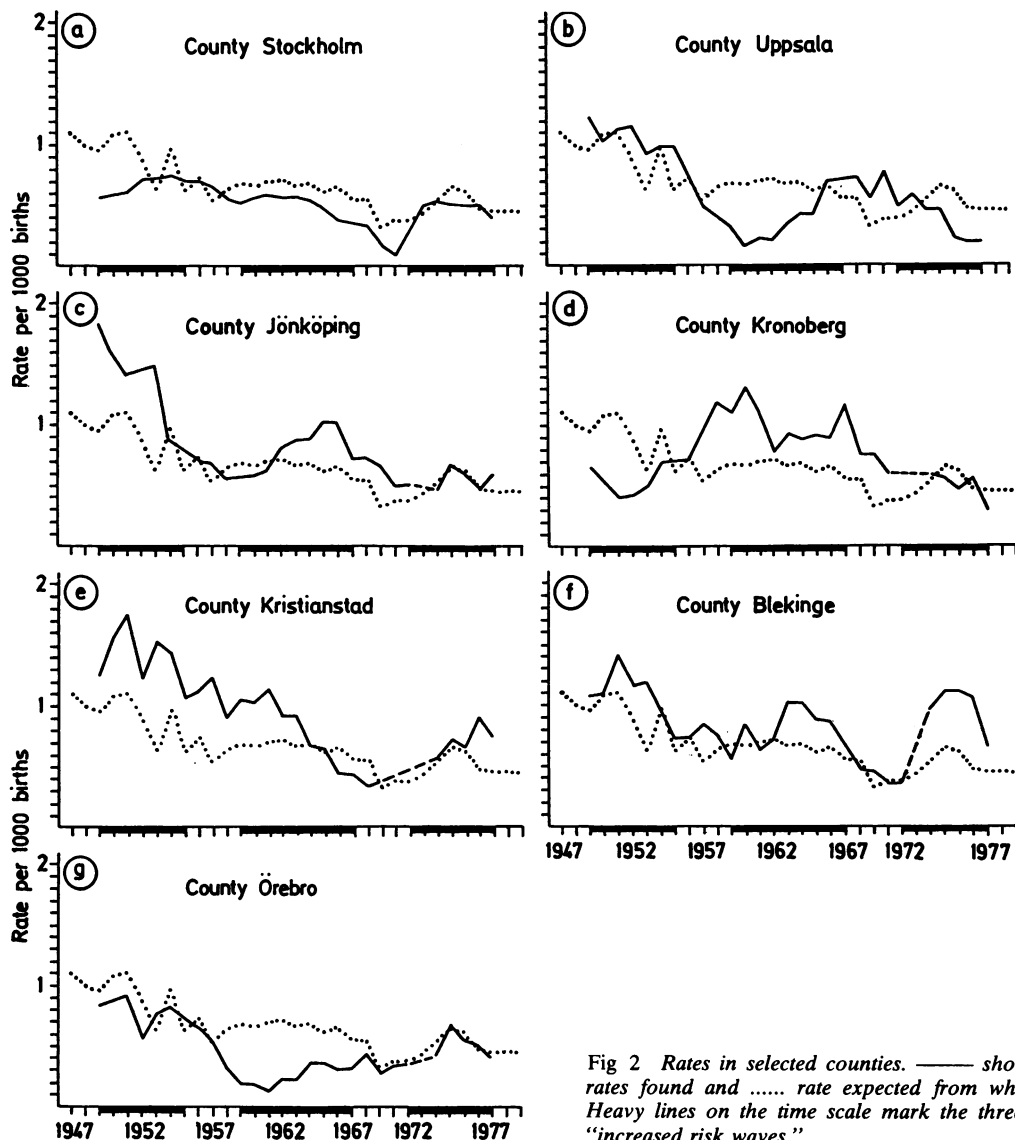


Fig 2 Rates in selected counties. — show the actual rates found and rate expected from whole country. Heavy lines on the time scale mark the three periods of "increased risk waves."

1970 but starting from a higher value than in the total country ending with an average rate, while Kronoberg county (county G, fig 2 D) behaves differently: starts with a rather low rate and shows an excess of cases from the middle of the 1950s to 1970.

To get a geographical distribution of high rates areas within Sweden, three maps were prepared (fig 3). For each map, areas with an excess of at least 2 per 10 000 are marked hatched and areas with an excess of at least 5 per 10 000 are marked black. Each map

represents one of the three "increased risk" periods: 1949–55, 1959–67, 1971–7.

There is a striking dominance of surplus areas among the Western counties in 1949–55 while a shift appears to have occurred to the southern counties for the 1959–67 period. Some counties appear as increased risk areas in both periods—for instance, Jönköping and Kronoberg—and one (Blekinge) remains high also in the third period. In the third period the county of Sörmland (county D) shows up

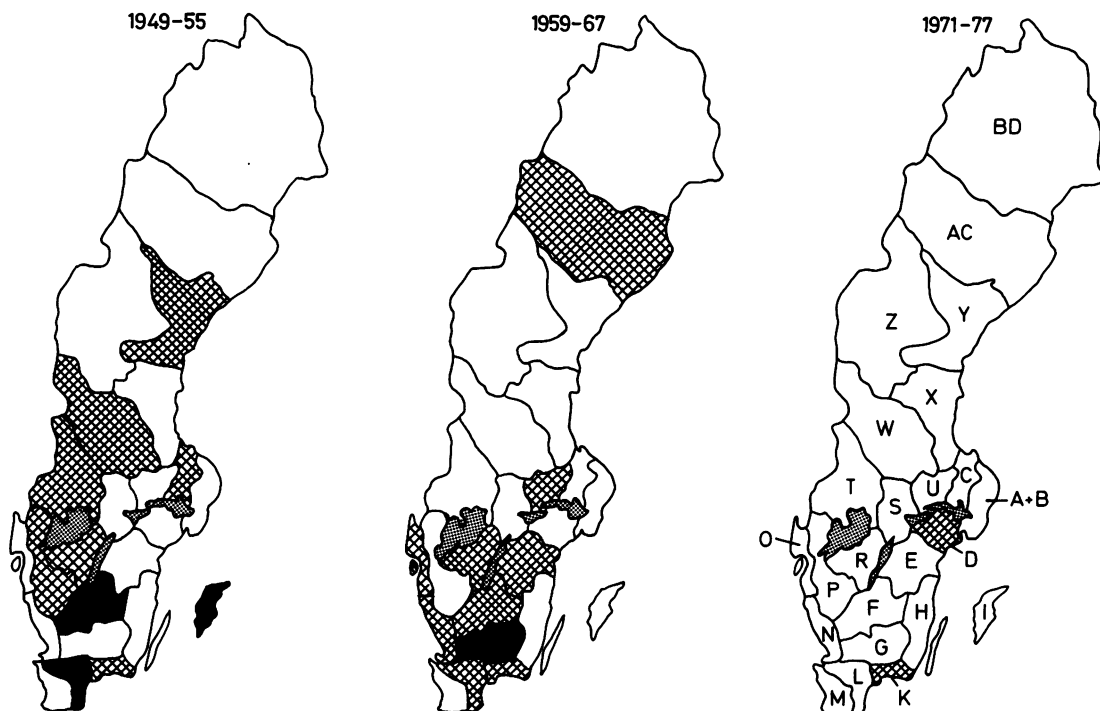


Fig 3 Three maps of Sweden, showing areas with increased rates of spina bifida under each one of the three "increased risk waves". Dotted areas are big lakes; black areas represent counties with a surplus of more than 5 per 10 000 births during the period in question; hatched areas represent counties with a surplus of between 2 and 5 per 10 000 births. White areas lie below that level. In third map (1971-7) lettering gives location of each county from the table.

to be the second high prevalence area, one of the extreme low prevalence areas during the previous period. The table gives the actual differences between found and expected rates for each county for each period. It should be noted that some of the rate differences are based on rather few cases: the county of Gotland (county I) for instance, marked black in fig 3, may well be a randomly high area as only nine cases occurred.

Discussion

The decline in spina bifida rate in Sweden described in the present paper resembles that seen in other parts of the world. Janerich found a decrease in New York State from 1.7 per 1000 births in 1945-7 to 0.6 per 1000 births about 1970.² The corresponding figures found in our study is about 1.1 in 1947 to 0.4 in 1970. The differences could be explained by poor ascertainment in the yearly report, but the figures obtained from that source agree well with the figures in the Register of Congenital Malformations, which has an 80-90% ascertainment of this malformation.

Differences among registered rates of spina bifida per 10 000 births in different counties in Sweden and the country mean rate. The three time periods represent the three "waves" of increased rate.

County	1949-53	1959-67	1971-7
Stockholm (A,B)	-0.9	-0.3	0.2
Uppsala (C)	3.5	-2.2	-1.2
Sörmland (D)	0.5	-1.4	3.6
Östergötland (E)	-0.7	3.5	1.3
Jönköping (F)	5.8	2.9	0.8
Kronoberg (G)	-3.7	5.1	0.0
Kalmar (H)	0.7	0.5	1.7
Gotland (I)	10.0	-2.7	0.2
Blekinge (K)	4.3	2.4	4.6
Kristianstad (L)	9.7	2.4	1.9
Malmö, Malmöhus (M)	-0.5	1.8	1.0
Halland (N)	1.6	3.2	1.4
Göteborg and Bohus (O)	1.5	3.8	1.5
Älvsborg (P)	2.7	1.5	0.2
Skaraborg (R)	2.4	3.2	1.1
Värmland (S)	4.0	1.2	0.5
Örebro (T)	1.9	-3.3	-0.1
Västmanland (U)	0.9	2.1	0.4
Kopparberg (W)	4.8	-1.5	0.7
Gävleborg (X)	0.1	0.8	1.1
Västernorrland (Y)	3.7	1.6	0.4
Jämtland (Z)	-0.5	-1.3	1.5
Västerbotten (AC)	-2.2	2.8	0.9
Norrboten (BD)	1.9	-0.1	-1.6

Furthermore, birth records as used by Janerich usually do not give a complete ascertainment. More probably there is an actual difference in prevalence in the two areas studied but, despite this, relatively parallel declines are seen. We noticed a temporary increase in the middle of the 1960s—the same phenomenon is indicated in the graphs given by Janerich.

There is a multifactorial aetiology of spina bifida (and other forms of NTD). A polygenic inheritance plays a part but there is ample evidence also for the significance of environmental factors, although few specific such factors have been identified. The baseline of spina bifida rates in a population would be determined by its genetic load, environmental factors can change the actual rate above the baseline level. It is more difficult to hypothesise that pronounced changes in the genetic load can occur in a population during a relatively short time to explain the observed changes. It is easier to understand how non-genetic factors could produce such changes. Many such factors have been described; during the past few years, some emphasis has been put on vitamin deficiency. The continuously improved health and socioeconomic situation of the population would be compatible with a decreasing NTD rate. This factor may not explain short term fluctuations in the rate changes noted in different parts of Sweden in this study. The socioeconomic structure of the population in Sweden is relatively uniform, and it is hard to believe that such factors could cause local variations in time trends. It is even more difficult to envisage sudden changes in the gene pools of the various areas which could explain the variations.

If one wants to look for an environmental hypothesis which could explain the noted changes, one would have to search for one or more factors, common in the western part of Sweden in the late 1940s and early 1950s, common in the south of Sweden in the first part of the 1960s and affecting part of central Sweden in the 1970s. It is not easy to suggest candidate(s) for this. It would have been interesting to locate each woman who gave birth to an infant with spina bifida to her actual place of living and study her general environment but unfortunately this cannot be done without an enormous amount of work before the time the central registers were started. Cases and controls from the middle of the 1970s (when the third peak occurred) can easily be

selected, however, and a regular case-control study on environmental factors can be made. Such a study is under way.

In fig 1 there is an indicated increase in rate seen in 1981. This may well be random, but a similar observation was recently reported from Hungary¹⁴ (this could also be random as it is based on few cases). The next few years will show if the rate continues to increase and if a new peak will be obtained.

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