Preventability of Neonatal Cold Injury and Its Contribution to Neonatal Mortality

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When the body temperature of a small neonate falls below 35 °C, latitude can be noted; severe derangements of cardiovascular, renal, hepatic, immunological, and hematological systems may also occur depending in part on the duration and severity of hypothermia. Diagnosis requires a low-reading thermometer, lacking which the diagnosis can be suspected, but most often is missed. Fatal cases of diagnosed cold injury commonly have terminal pneumonias or sepsis. Prevention involves identification and home visits to high-risk infants; intensive care of those with the diagnosis at Soroka Hospital Medical Center has reduced the case-fatality rate from 30% in 1971 to 3% in 1988–1989. During the same period in our region, the proportion of neonatal deaths occurring in winter months of December, January, and February has dropped from 55 to 27%. The expected proportion is 25%. We hypothesize that excess neonatal mortality during winter months, especially due to pneumonia and sepsis or sudden infant death syndrome (SIDS) is an indicator of missed cold injury syndrome.

A preliminary evaluation was made from U.S. data by state, provided by the National Center for Health Statistics, which records no fatalities from cold injury during 1986. Contrasted with this are 26 cold injury deaths in Israel for 1977–1980. In the U.S., though, excess winter neonatal deaths in 1986 from SIDS, pneumonia, and sepsis are reported. These deaths amount to 13 of 368 deaths attributed to SIDS and 8 out of 158 deaths from influenza and pneumonia and 7 out of 770 deaths from sepsis; however, from the states of North Carolina, South Carolina, Mississippi, Virginia, and Pennsylvania, the excess is about 21 deaths compared to the yearly number in these states of 219 from these causes. These states also have substantial portions of the population with poor education and substandard housing. The use of low-reading thermometers in a randomized clinical trial in such states would be justified. These findings are consistent with a possible reduction of about 10% in selected causes of neonatal mortality from an active program of detection of neonatal cold injury under high-risk conditions.

Introduction

Neonatal hypothermia was first designated “cold injury” by Nassau in 1948 (1), but even earlier, infants with the same type of damage to the skin were designated as sclerema neonatorum by Underwood in 1811, who noted that babies presenting with induration of subcutaneous tissue had a low body temperature and a poor prognosis (2).

Mann and Elliot in 1957 wrote (3):

Commonly the disorder is misdiagnosed as hemorrhagic pneumoniuu or sclerema, the predominant role of exposure to cold being overlooked. Cases generally arise after home confinements, especially in severely cold weather. . . . Presenting features may include increasing apathy, food refusal, coldness to touch and oliguria: but the infant does not look ill. The most constant clinical findings are hypothermia, oedema of the extremities, purulent nasal discharge, and striking skin erythema. The treatment advised is slow rewarming, liberal glucose administration by intragastric drip, and antibiotic cover.

Subsequent studies have been reported from Scotland, and seemingly paradoxically from a variety of subtropical countries, such as Israel, Ethiopia, India, and Iraq (4–9). The seeming paradox is related to the fact that in these subtropical countries, cold nights are exceptional and therefore supplemental heat in sleeping rooms is not usually needed for adults. In addition, in these countries, many mothers are poorly educated.

Only four cases have been reported from the U.S. in the periodical literature. In the U.S. Vital Statistics for 1986, there were no deaths for which ICD-9 no. 778.2, “cold injury syndrome” (CIS) was the principal cause of death, although the condition was mentioned, but not considered the underlying cause of death on one certificate.

In the U.S. in 1987 there were 368 neonatal deaths attributed to sudden infant death syndrome (ICD-9, 798.0), whereas in Israel for 1977–1980 among all infant deaths, 26 were attributed to 778.2, while 99 were attributed to SIDS. If we limit the comparison in Israel to neonatal deaths the ratio of CIS deaths to SIDS deaths would be greater. There are subtropical areas of the U.S. with mothers of low educational level and cold snaps. CIS deaths must be occurring in the U.S., but are not being recognized. Unless CIS is recognized, it will not be prevented, and, as we will show, CIS is preventable. We will look at possible indices that suggest where and when to look.

Natural History of Cold Injury Syndrome

Several studies in Israel called attention to important features of the natural history of CIS. Cohen (4) called attention to the importance of coagulation abnormalities. Dagan and Gorodischer

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(10) reported on the frequency of infection among hypothermic infants. Meanwhile, a debate was going on as to whether it was preferable to rapidly or slowly warm the infants. Sofer et al. (11) reviewed the hospitalization of 56 hypothermic infants seen at Soroka Medical Center over three winters. They reported:

One or more severe associated disturbances, including metabolic abnormalities, bleeding tendency, infection and respiratory failure were observed in most cases. 38 received slow warming, but 18 of the worst cases received rapid warming. These 18 were among the 24 cases treated in a pediatric intensive care unit. Fourteen required assisted mechanical ventilation. 53 of the 56 survived, and of the three who died none was rapidly warmed, and two had severe underlying central nervous system infection.

Thus, the natural history begins with a drop of body temperature below 35°C, which if continued or aggravated, leads to clotting deficiency, severe hypoglycemia, cardiac, respiratory, or renal failure, complicated by infection or pneumonia. Rewarming may fail to reverse these, and death may ensue, which may be attributed to SIDS, pneumonia, or some type of infection. Treatment of the failing bodily symptoms and antibiotics provide the best chances for survival, regardless of the rate of rewarming. Figure 1 shows the age at diagnosis of Jewish and Bedouin infants in the Negev in 1987–1989, and Figure 2 shows the month of diagnosis for the same infants.

**Hypothesis**

It must follow that if in the presence of recognized hypothermia (24–34°C), one or more severe disturbances are found, if the hypothermia is not recognized, these severe abnormalities would still be present and without vigorous treatment, are likely to be fatal. Under these circumstances, pneumonia, sepsis, respiratory failure, or SIDS are the most likely diagnoses.

This hypothesis will be examined under two circumstances. First, as CIS becomes more consistently recognized (and treated) in the Negev, we will look to see what happens to mortality from pneumonia, sepsis, respiratory failures and SIDS in the neonatal period. A parallel examination will be made for the residents of the Gaza Strip. If indeed, winter excess deaths from these conditions drops as CIS in recognized and treated or prevented, it will suggest that some cases of CIS may have been missed in the earlier period but not in the later period.

Second, we will examine the neonatal mortality data for U.S. by state for the year 1986, looking for winter excess in such diagnoses as discussed previously. In locations with such a winter excess, it is reasonable to suspect that missed CIS is the cause, and an attempt to identify it would be justified.

**Observations on Cold Injury in the Negev (South) of Israel**

The incidence of cold injury among infants has been a matter of serious concern among public health nursing personnel in the Negev Regional Office of the Ministry of Health for nearly 15 years. The nurses are equipped with low-reading thermometers (Fig. 3) and as part of the routine postnatal care, make home visits, with special attention being given to babies with small birth weight during the periods of cold weather. When babies with a body temperature of 34°C or less are identified, they are sent to the Soroka Hospital Medical Center.

Dagan and Gorodischer (10) reported on 51 such infants who were less than 3 months old and admitted during the years of 1976 through 1981. Twenty-eight were males and 23 females; 41 were admitted during the first month of life. Forty-three of them were from rural areas and villages, and 8 were born at home rather than in the hospital. Thirty-four were at least partially breast fed at the time of admission. Twenty-seven of them had some evidence of infection.

All were within the first 10th percentile of weight for age, and 11 had diarrhea and dehydration. The tendency to dehydration was evidenced by the high prevalence of elevated hematocrit (34 greater than 16 g hemoglobin/dL). Six died, of which 5 had infection.

A further 56 hypothermic infants were observed in the Soroka Hospital by Sofer et al., covering the period from November 1, 1982, to October 31, 1985 (11). Of these, 29 were Bedouin and 27 Jews, which represents a slight shift toward Jews compared to 29 Bedouin and 22 Jews studied by Dagan and Gorodischer (10). Forty-six of the babies studied by Sofer et al. were seen during the first 30 days of life (11). In contrast to the mortality rate of hospitalized infants prior to 1974, which was 31%, only 3 of the infants treated by Sofer et al. succumbed (11).

During the two winters, 1987–1988 and 1988–1989, the Public
Table 1. Diagnosis of cold injury syndrome.

| Symptom/Symptoms                              | Temperature lower than 35°C* |
|----------------------------------------------|-----------------------------|
| Complications of cardiovascular impairment   |                            |
| Complications of pneumonia, sepsis           |                            |

*Only low body temperature is diagnostic.

Table 2. Risk factors for cold injury by host and by environment.

| Host          | Environment               |
|---------------|---------------------------|
| Poor education| Temperature < 5°C         |
| First births  | Unheated housing          |
| Home delivery | Swaddling (?)             |
| Scant prenatal care |                   |
| Low birth weight |                      |

Table 3. Neonatal deaths by month in the Negev of Israel by time period and for cold injury (CIS) or pneumonia and sepsis (PS). *

| Month | 1971–1973 | 1977–1980 | 1983–1985 |
|-------|-----------|-----------|-----------|
|      | Total CIS| Total CIS| Total CIS|
|      | 1981–86  | 1986–88   |           |
| Jan  | 14       | 8         | 2         |
| Feb  | 14       | 7         | 3         |
| Mar  | 5        | 7         | 1         |
| Apr  | 7        | 5         | 1         |
| May  | 6        | 6         | 0         |
| Jun  | 4        | 4         | 0         |
| Jul  | 3        | 6         | 0         |
| Aug  | 4        | 9         | 0         |
| Sep  | 5        | 9         | 1         |
| Oct  | 7        | 4         | 0         |
| Nov  | 4        | 9         | 0         |
| Dec  | 3        | 12        | 2         |
| Total| 56       | 89        | 20        |

*Excluding deaths from prematurity, birth injury, or congenital abnormality.

Figure 3. A low-reading thermometer.

Health Nurses identified 61 incident cases, of which 55 were under 30 days of age; 29 were Jewish and 32 Bedouin. Of these, 24 Jews and 31 Bedouin were hospitalized. The estimated annual rates were for Jews, 2.4/1000 live births in 1987–1988 and 1.7 in 1988–1989, and for Bedouin, 8.0 for 1987–1988 and 4.8 for 1988–1989. Of this group there were 2 deaths.

If one restricts the consideration to high-risk infants born during cold weather, the incidence may be as high as 3%. Table 1 shows the criteria for diagnosis of CIS. Table 2 shows the risk factors for cold injury by host and environment.

Table 3 shows the monthly incidence of neonatal deaths due to CIS and to pneumonia and sepsis in the Negev for 1971–1973.

Figure 4. Proportions of neonatal deaths in winter months of December, January, and February for various time periods and attributed to various causes. Solid bars, cold injury; hatched bars, pneumonia and sepsis; dotted bars, neonatal deaths. The proportion of cold injury deaths in the winter is expected to be high, and the proportion and numbers are shown. The proportion attributed to pneumonia and sepsis and the proportion of all neonatal deaths occurring during these months has dropped toward the expected value of 25% as the effectiveness of case-finding and prevention of cold injury has improved.

Figure 5 shows the monthly incidence of these deaths that occur during the winter months of December, January, and February. Figure 5 shows the monthly incidence of these data for two time periods for the population of the Negev, and Figure 6 shows similar data for the Gaza Strip.
Data for the U.S., 1986 and 1987

Table 4 shows the 20 states of the U.S. with elevated neonatal mortality rates in 1986, along with the numbers of such deaths, as well as the numbers in 1987 attributed to SIDS (ICD 798.0), influenza and pneumonia (ICD 480–487), and to other infections specific to the perinatal period (ICD 771.8). This latter category is elsewhere identified as “sepsis.” The District of Columbia had the highest neonatal death rate and is included although not strictly a state.

The expected numbers of winter deaths can be obtained by multiplying the denominator data by 90/365 = 0.2466, the proportion of days in the year that occurs in the three winter months of December, January, and February. The 20 states with neonatal mortality above the U.S. average shown in Tables 4 and 5 account for 18 of the 28 excess neonatal deaths, indicating that total neonatal mortality is not a very strong predictor of winter excess neonatal mortality from these causes. Of course, statewide data

Table 4. Neonatal deaths and neonatal death rates for the U.S. and for states with elevated neonatal rates, 1986, and numbers of neonatal deaths attributed in 1987 to SIDS, influenza and pneumonia, and to other infections specific to the perinatal period.*

|                | 1986 |                | 1987 |
|----------------|------|----------------|------|
|                | Neonatal deaths | Neonatal rate/100,000 live births | SIDS | Pneumonia and flu | Other infections |
| U.S.           | 25,212 | 6.7            | 368  | 158             | 770             |
| District of Columbia | 162  | 16.1           | 0    | 0               | 5               |
| Alabama        | 541   | 9.1            | 12   | 3               | 19              |
| Delaware       | 86    | 8.8            | 2    | 1               | 2               |
| South Carolina | 456   | 8.8            | 3    | 4               | 17              |
| Georgia        | 835   | 8.5            | 10   | 8               | 27              |
| Maryland       | 576   | 8.3            | 8    | 2               | 14              |
| Illinois       | 1437  | 8.1            | 25   | 16              | 42              |
| Louisiana      | 605   | 7.8            | 9    | 7               | 22              |
| Michigan       | 1080  | 7.8            | 15   | 5               | 24              |
| North Carolina | 691   | 7.7            | 14   | 3               | 32              |
| Mississippi    | 324   | 7.7            | 9    | 2               | 19              |
| Vermont        | 61    | 7.5            | 2    | 0               | 1               |
| Indiana        | 597   | 7.5            | 11   | 3               | 21              |
| Virginia       | 651   | 7.5            | 10   | 3               | 13              |
| Florida        | 1652  | 7.5            | 10   | 12              | 34              |
| New York       | 1937  | 7.3            | 19   | 10              | 54              |
| Ohio           | 1086  | 6.9            | 11   | 3               | 32              |
| Tennessee      | 457   | 6.9            | 10   | 1               | 22              |
| Pennsylvania   | 1092  | 6.8            | 23   | 6               | 47              |
| Connecticut    | 303   | 6.8            | 1    | 1               | 8               |
| Missouri       | 512   | 6.8            | 11   | 1               | 14              |

*Source: H. Rosenberg, National Center for Health Statistics (personal communication).

Table 5. Proportion of neonatal deaths due to SIDS, pneumonia or influenza, or sepsis which occurs during the winter months of December, January, and February, 1987, in the U.S. and in states with high neonatal mortality.*

|                | SIDS | Pneumonia | Sepsis | Total | Percent |
|----------------|------|-----------|--------|-------|---------|
| U.S.           | 104/368 | 47/158  | 197/777 | 348/1296 | 26.9    |
| District of Columbia | 0    | 0         | 1/5    | 1/5   | 20.0    |
| Alabama        | 4/12 | 0/3       | 2/19   | 6/34  | 17.6    |
| Delaware       | 1/2  | 1/1       | 1/2    | 3/5   | 60.0    |
| South Carolina | 1/3  | 2/4       | 6/17   | 9/24  | 37.5    |
| Georgia        | 5/10 | 1/8       | 4/27   | 10/45 | 22.2    |
| Maryland       | 3/8  | 0/2       | 3/14   | 6/24  | 25.0    |
| Illinois       | 4/25 | 4/16      | 12/20  | 20/83 | 24.1    |
| Louisiana      | 3/9  | 1/7       | 7/22   | 11/38 | 28.9    |
| Michigan       | 4/15 | 1/5       | 3/24   | 8/44  | 18.2    |
| North Carolina | 6/14 | 1/3       | 12/32  | 19/49 | 38.8    |
| Mississippi    | 4/9  | 1/2       | 7/19   | 12/30 | 40.00   |
| Vermont        | 0/2  | 0/1       | 0/3    | 0.0   |         |
| Indiana        | 2/11 | 0/3       | 4/21   | 6/35  | 17.1    |
| Virginia       | 4/10 | 0/3       | 5/13   | 9/26  | 34.6    |
| Florida        | 1/10 | 6/12      | 9/34   | 16/56 | 28.6    |
| New York       | 5/19 | 3/12      | 15/54  | 23/85 | 27.1    |
| Ohio           | 5/11 | 0/3       | 7/32   | 12/46 | 26.1    |
| Tennessee      | 2/10 | 1/1       | 2/22   | 5/33  | 15.2    |
| Pennsylvania   | 5/23 | 3/6       | 16/47  | 24/76 | 31.6    |
| Connecticut    | 0/1  | 1/1       | 3/8    | 4/10  | 40.0    |
| Missouri       | 3/11 | 1/1       | 2/14   | 6/26  | 23.1    |
| Total          | 62/215 | 27/93    | 121/469 | 210/77 | 27.0    |

*Source: H. Rosenberg, National Center for Health Statistics (personal communication).
can obscure more striking problems in a low-income, badly housed minority group. The data show more striking effects for the first two categories, SIDS and influenza and pneumonia, than for the category designated as "sepsis." For New York City, to take an example, the data for SIDS are 4/9, for influenza and pneumonia 2/7, and for sepsis 7/32. For the SIDS and influenza and pneumonia, together, the winter ratio is 6/16 or 37.5%, whereas for the state including New York City, it is 8/31 or 25.8%.

Overall, there are about 28 excess winter neonatal deaths from these three causes in the U.S. About half are due to SIDS and about equal numbers but proportionally more due to influenza and pneumonia than to sepsis.

The excess is greater in states of the southeastern region, where other risk factors for cold injury are likely to be high. A clinical trial of the use of low-reading thermometers in such states would be justified.

Discussion

Most of cases of SIDS occur after the neonatal period, so it must follow that only a small proportion of the otherwise unexplained sudden infant deaths could be due to undiagnosed cold injury. According to our hypothesis, that proportion would be greatest in winter and in locations with high risk populations. Neonatal mortality data by state in the U.S. must include many deaths due to immaturity and congenital abnormalities, as well as deaths from populations not at high risk. Despite this dilution, the data suggest that as much as 10% of neonatal deaths attributed to SIDS or to influenza or pneumonia in certain states may be actually due to unrecognized cold injury. Since we have shown that deaths from cold injury, and to some extent, morbidity from cold injury, are preventable, the effort to detect and prevent these deaths seems worthwhile.

We suggest that a clinical trial be conducted in order to see if detection of CIS can be accomplished. The trial would involve introducing the use of low-reading thermometers to nurses in randomized jurisdictions with excess neonatal deaths in winter months.

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