Poikilothermia and Susceptibility of Suckling Mice to Coxsackie B1 Virus

INFECTIONS with most types of Coxsackie virus are fatal to newborn mice in normal conditions. This susceptibility decreases sharply with age and, when the mice are a few days old, the infection runs a subclinical course[1]. As yet no satisfactory explanation of this phenomenon has been offered.

A greater susceptibility to some virus infections occurs if the temperature of the host is reduced and adult mice which are made hypothermic become susceptible to Coxsackie virus[2].

In most newborn animals there is a physiological hypothermia and poikilothermia[3]. We therefore studied the possible influence of body temperature on the susceptibility of newborn mice to Coxsackie virus.

The body temperature was measured in suckling mice varying in age from 12 h to 10 d. The mice were kept in cages held at room temperature (22 to 24°C). The body temperature was measured in the peritoneal cavity by insertion of a thermister. Each point in Fig. 1 indicates the average temperature of thirty to fifty suckling mice. The temperature was measured of mice taken directly from the nest with the mother on the nest, and it was ensured that she had stayed there for a period of at least 10 min. The temperatures measured 10 min and 20 min after the mother had been taken away from the nest are also shown. The babies were left piled just as when the mother normally leaves the nest. Each mouse was used for measuring one temperature only.

As the influence of poikilothermia on the course of infection is obviously related to the behaviour of the mothers, this was followed for a total of 6,360 min; twenty-two litters for 180 min in daylight and twenty litters for 120 min in twilight. The mothers were found to be away from the nest for an average total of 49% of the time (55% in twilight and 45% in daylight). Absences for periods longer than 10, 20 and 30 min, respectively, were recorded as 42%, 31% and 20% of the time. Concerning these longer absences, no significant differences could be found between daylight and twilight.

The hypothermia and, particularly, the poikilothermia found in newborn mice thus decreased within a few days. At an age of 9 to 10 d, the mice had a temperature, with their mother on the nest, just as high as adult mice. The poikilothermia decreased especially after about 6 d. The effect of this decrease was pronounced, particularly when the mothers were kept away for relatively long periods, and is in agreement with previous results[4].

The mortality of suckling mice caused by Coxsackie B1 virus in relation to the age at which the mice were infected was also studied and is given in Fig. 1. The mice were infected intraperitoneally with a dose of 60 LD_{50} (titrated intracerebrally in 1-d-old mice). An abrupt decrease in mortality occurred around day 6, and after day 8 no mortality was seen with this dose of virus. This result is also in agreement with a previous report[5].

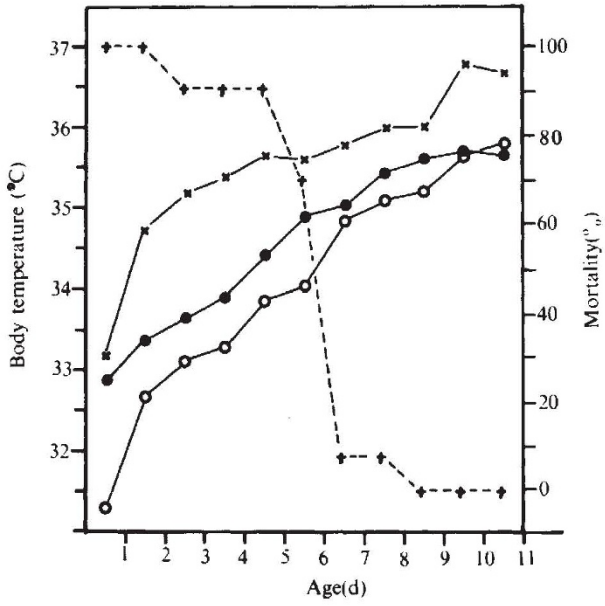

Fig. 1 Body temperature in suckling mice of varying age. The temperature was measured on mice taken directly from the nest with the mother on the nest, and it was ensured that she had stayed there for at least 10 min (×). The temperatures measured 10 min (●) and 20 min (○) after the mother had been taken away from the nest. The mortality in relation to the age at which the mice were infected (+).

Table 1 Results of various experiments in which infected and uninfected newborn mice were placed at ambient temperatures of 22 to 24° C and 34° C.

Experiment No.	Age (d)	Inoculation: Virus dose	Inoculation: Route	Mortality at ambient temperature: 22 to 24° C	Mortality at ambient temperature: 34° C
1	1.5	60 × LD_{50}	Intracerebral	6/7	1/7
2	0.5	60 × LD_{50}	Intracerebral	6/7	3/7
3	1.5	60 × LD_{50}	Subcutaneous	7/7	1/7
4	2	60 × LD_{50}	Intraperitoneal	12/12	1/12
5	2	60 × LD_{50}	Intraperitoneal	10/10	3/20
6	1.5	60 × LD_{50}	Intraperitoneal	5/5	1/5
7	3	60 × LD_{50}	Intraperitoneal	10/10	3/25
8	3	No virus	—	—	0/20
9	1.5	No virus	Phosphate buffered saline (intraperitoneal)	—	4/20

To study the mortality of newborn mice in which the body temperature was stabilised around the lowest body temperature of the baby mice which survived, that is, 9 to 10-d-old babies, the cages with the mothers and their 1 to 3-d-old babies infected with a dose of 60 LD_{50} Coxsackie B1 virus were placed in an incubator at 34° C. The average body temperature of newborn mice kept in these conditions was found to be 35.8° C throughout the experiment. At this temperature, the suckling mice were lying free in the cage and were never found nesting. Table 1 shows the results of various experiments which revealed a pronounced reduction in mortality in mice with this body temperature throughout the course of infection.

Thus a correlation between poikilothermia and susceptibility to Coxsackie B1 virus was found. The higher temperature in the older mice might inhibit viral infection by decreasing virus replication in infected cells or by potentiating host defence mechanisms. Obviously the destruction of cells by growth of virus may also be different in hypothermic and normothermic conditions. Further evaluation of these possibilities is in progress in this laboratory.

BØRGE TEISNER
SVEN HAAHR

Institute of Medical Microbiology,
University of Aarhus,
8000 *Aarhus C*

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