

# Circadian and seasonal factors in the pathogenesis of acute myocardial infarction: the influence of environmental temperature

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## Abstract

**Objective**—To determine the circadian and seasonal variations in the incidence of acute myocardial infarction and the influence of environmental temperature.

**Patients**—633 consecutive patients with acute myocardial infarction admitted to a coronary care unit over four years.

**Setting**—Coronary care unit in a district general hospital.

**Design**—An observational study.

**Results**—The onset of acute myocardial infarction had a circadian rhythm with a peak in the second quarter of the day. A seasonal variation was also found with a significant winter peak. There was, however, an excess of infarctions on colder days in both winter and summer indicating that the effect of environmental temperature on the onset of acute myocardial infarction is independent of the time of year.

**Conclusion**—Acute myocardial infarction is more common in winter and more common on colder days, independent of season. Environmental temperature may play an important part in the pathogenesis of acute myocardial infarction.

(Br Heart J 1993;69:385-387)

Circadian and seasonal rhythms are recognised in many physiological systems. Catecholamines, for example, have a circadian rhythm with a morning peak and nocturnal trough, whereas mood is known to vary with the seasons.

Over recent years, similar patterns have been sought and established in ischaemic heart disease. Several studies have shown that a circadian rhythm occurs in myocardial infarction<sup>1</sup> as well as in myocardial ischaemia<sup>2</sup> and sudden cardiac death,<sup>3</sup> although the mechanisms are unclear. Seasonal rhythms in ischaemic heart disease, however, have been more difficult to establish. Thus a winter peak in mortality has been reported in both the United Kingdom and in Canada,<sup>4</sup> but this was based on analysis of death registration data, which are notoriously inaccurate.<sup>5</sup> There is little information on seasonal variation in the incidence of acute myocardial infarction<sup>6,7</sup> and data on the role of environmental temperature are conflicting. More infarcts occurred on colder days in the sub-arctic climate of northern Finland,<sup>8</sup> but temperature did not seem to influence the onset

of acute myocardial infarction in the temperate climate of Tasmania.<sup>9</sup>

In our study, therefore, we have analysed the seasonal variation of acute myocardial infarction in a London borough, with particular reference to the influence of environmental temperature.

## Patients and methods

### PATIENTS

The study group comprised 633 consecutive patients with acute myocardial infarction admitted to the coronary care unit of Newham General Hospital over a four year period from 1 January 1988 to 31 December 1991. The mean age of patients was 62 years (range: 26 to 94) and 462 were male. The diagnosis of acute myocardial infarction was based on any two of the following three criteria: (a) cardiac chest pain lasting at least 30 minutes; (b) electrocardiographic changes of myocardial infarction with  $\geq 1$  mm ST elevation in two or more contiguous limb leads or  $\geq 2$  mm ST elevation in two or more contiguous chest leads; (c) a diagnostic rise in creatine kinase ( $\geq 400$  IU/l).

The date and time of onset of chest pain were documented at the time of admission. Weather conditions for each day over the four year study period were obtained from the London Weather Centre. To find the influence of environmental temperature, the minimum temperature on the day of infarction for each of the 633 patients was noted as well as the minimum temperature on each day during the four year study period. The minimum temperature for each day was defined as the minimum temperature during the 12 hours before 0900.

For comparison of seasonal changes in the local population, we undertook a separate analysis of the incidence of acute appendicitis over the same period. Data were taken from the surgical register of the operating theatre.

### DATA ANALYSIS

Circadian variation was examined by calculating the number of patients whose pain started in each of twelve two hour periods throughout the day. For seasonal and temperature variation admission rates to the hospital were calculated by month and temperature band. Tests of heterogeneity and linear trend were applied.<sup>10</sup> Ninety five per cent confidence intervals (95% CIs) were derived from tabulations of the Poisson distribution.

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Accepted for publication  
21 December 1992

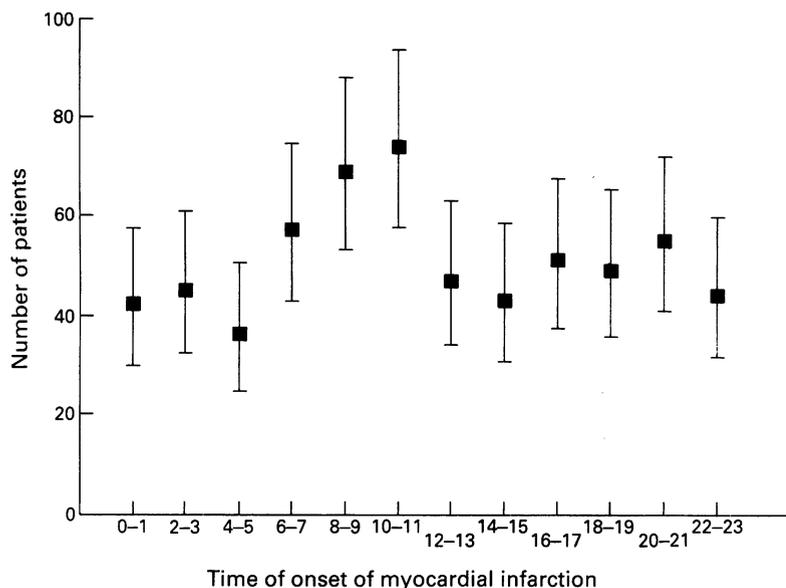


Figure 1 Distribution of time of onset of symptoms of acute myocardial infarction ( $n = 612$ ) by 12 two hour periods with 95% CIs. Test for heterogeneity:  $\chi^2 = 25.9$  on 11 degrees of freedom (df),  $p = 0.007$ .

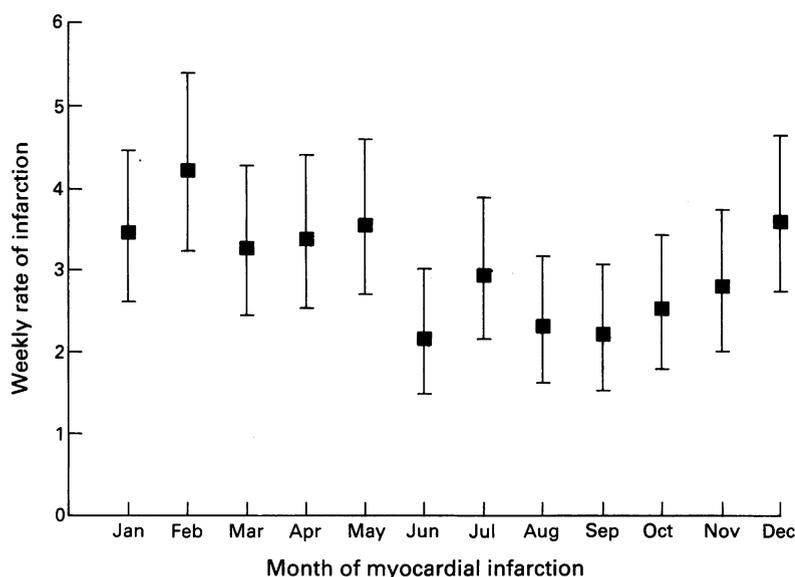


Figure 2 Occurrence of acute myocardial infarction each month ( $n = 633$ ) with 95% CIs. Test for heterogeneity:  $\chi^2 = 26.0$  on 11 df,  $p = 0.006$ .

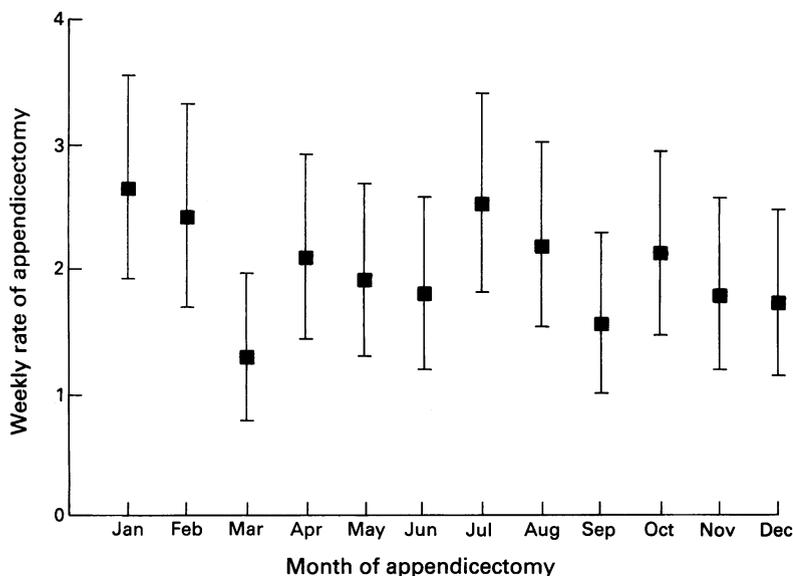


Figure 3 Occurrence of appendicectomy each month ( $n = 421$ ) with 95% CIs. Test for heterogeneity:  $\chi^2 = 15.6$  on 11 df,  $p = 0.2$ .

Table 1 Number of days and number of acute myocardial infarctions (MI), occurring in each of six temperature bands, over a four year period

Temperature ( $^{\circ}\text{C}$ )	Days	MI	Rate/week	(95% CI)
< 3.0	99	65	4.60	(3.55 to 5.86)
3.0-5.9	239	110	3.22	(2.65 to 3.88)
6.0-8.9	285	137	3.36	(2.83 to 3.98)
9.0-11.9	322	131	2.85	(2.38 to 3.38)
12.0-14.9	288	113	2.75	(2.26 to 3.30)
$\geq 15.0$	228	77	2.36	(1.87 to 2.95)

Test for heterogeneity:  $\chi^2 = 18.5$  on 5 df,  $p = 0.002$ , test for linear trend:  $\chi^2 = 15.4$  on 1 df,  $p < 0.001$ .

## Results

### CIRCADIAN VARIATION

The time of onset of pain was known in 612 patients (fig 1). There was significant variation in onset of infarction throughout the day, (test for heterogeneity:  $\chi^2 = 25.9$  on 11 degrees of freedom (df),  $p = 0.007$ ). The main peak occurred in the second quarter of the day (0600-1159), during which 31.6% of the group experienced the onset of symptoms.

### SEASONAL VARIATION

The hospital admission rate also showed significant seasonal variation (fig 2) with more admissions during winter than summer months. Thus 30.5% of the total study group presented in the three months from December to February. By contrast, acute appendicitis did not show seasonal variation (test for heterogeneity:  $\chi^2 = 15.6$  on 11 df,  $p = 0.2$ ) and as many patients were admitted between April and September (212) as between October and March (209) (fig 3).

### TEMPERATURE VARIATION

The admission rate for myocardial infarction was inversely related to the minimum daily temperature (table 1). The admission rate on days when the minimum temperature fell below  $3^{\circ}\text{C}$  was nearly double that found on days with a minimum temperature of  $15^{\circ}\text{C}$  or more.

To determine if the excess of infarction on colder days reflected a seasonal rather than a temperature effect, the winter months (October to March) and the summer months (April to September) were considered separately (table 2). The higher rate of infarction

Table 2 Number of days and number of acute myocardial infarctions (MI), occurring in each of five temperature bands, over a four year period, shown separately for winter and summer

Temperature ( $^{\circ}\text{C}$ )	Days	MI	Rate/week	(95% CI)
Winter 6 months				
< 3.0	89	57	4.48	(3.40 to 5.81)
3.0-5.9	192	91	3.32	(2.68 to 4.07)
6.0-8.9	209	94	3.15	(2.55 to 3.85)
9.0-11.9	163	59	2.53	(1.93 to 3.63)
$\geq 12.0$	72	43	4.18	(3.03 to 5.63)
Summer 6 months				
< 6.0	56	27	3.38	(2.22 to 4.91)
6.0-8.9	76	43	3.96	(2.85 to 5.36)
9.0-11.9	160	72	3.15	(2.46 to 3.97)
12.0-15.0	223	72	2.26	(1.77 to 2.85)
$\geq 15.0$	221	75	2.38	(1.87 to 2.98)

Test for heterogeneity for winter months:  $\chi^2 = 11.8$  on 4 df,  $p = 0.02$ , test for linear trend for winter months:  $\chi^2 = 1.88$  on 1 df,  $p = 0.17$ , test for heterogeneity for summer months:  $\chi^2 = 12.3$  on 4 df,  $p = 0.015$ , test for linear trend for summer:  $\chi^2 = 8.76$  on 1 df,  $p = 0.003$ .

on colder days was apparent for both summer and winter months but the trend was only significant in summer.

### Discussion

This study confirms a morning peak in the onset of acute myocardial infarction and a seasonal variation with more infarcts in the winter months. The mechanism of this seasonal variation is unknown, but it seems to be dependent on climatic variables. In the subtropical climate of New Orleans, for example, the incidence of acute myocardial infarction peaks during the summer<sup>7</sup> by contrast with the winter peak in our own more temperate climate. It has not been established, however, whether the variation between winter and summer is truly seasonal, or whether it depends on environmental temperature.

The temperature data showed an excess of infarcts on colder days, but this does not reliably distinguish between the effects of season and environmental temperature. By considering the summer and winter months separately, we were able to control for season and analyse the independent influence of temperature on the onset of acute myocardial infarction. The analysis confirmed a higher rate of infarction on colder days in both winter and summer, suggesting that under conditions of reduced environmental temperature the risk of acute myocardial infarction increases independently of time of year.

Mechanisms relating environmental temperature to the onset of acute myocardial infarction must remain speculative. Sympathetic tone may be important because it increases in the cold,<sup>11</sup> with several consequences. Heart rate and blood pressure tend to rise, increasing the myocardial oxygen demand. Haematological variables are also affected as reflected by increases in  $\beta$  thromboglobulin and platelet factor 4 that in turn enhance platelet aggregation.<sup>12</sup> These adverse haematological effects of sympathetic stimulation may to some extent be countered by changes in blood viscosity and packed cell volume that tend to be higher in patients presenting with acute myocardial infarction in the summer, compared with winter.<sup>13</sup>

Although there is a clear independent effect of temperature on the incidence of acute myocardial infarction, our analysis of seasonal effects has assumed that the population at risk remains the same throughout the year. This assumption may not be accurate because of seasonal changes caused, in particular, by annual holidays that are usually taken in the summer months. By choosing to exam-

ine the seasonal variation of acute appendicitis, we were able to obtain accurate data based on the surgical register of the operating theatre, and did not have to depend on Hospital Activity Analysis data, which are notoriously unreliable.<sup>14</sup> The incidence of acute appendicitis showed no seasonal changes and, importantly, there was no palpable reduction in the summer months, even though the population at risk is younger and probably more mobile than our study population. Thus any effect of seasonal population changes is likely to have been small.

In conclusion, therefore, this study suggests a seasonal variation in the incidence of acute myocardial infarction that is at least partly dependent on the environmental temperature. Myocardial infarction occurs more commonly on colder days, regardless of the time of year, indicating that environmental temperature may be an important variable in the pathogenesis of acute myocardial infarction.

BM is funded by the British Heart Foundation.

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