BMJ 1994;309:613 (3 September)

Chronobiology

This summer I had the opportunity to return to Bratislava for another meeting on chronobiology, the study of biological phenomena as they occur in time and exhibit a rhythm or periodicity. This relatively new discipline brings together students of statistics, mathematics, and even astronomy, as well as physicians concerned with hypertension, preventive medicine and epidemiology, neuroanatomy, sleep, psychiatry, and menstrual cycles. Then there is a further tendency for diverse interests to be brought together by common mechanisms at the cellular level. Here ionic fluxes, kinases, and transporting proteins give rise to innate rhythms, best exemplified by the contracting myocytes of the heart or the neurones controlling sleep. Such rhythms, moreover, can be further modulated by external factors. Thus a sunflower kept in the dark exhibits an innate rhythmical movement, which changes on exposure to light so that the plant's movements become synchronized with the solar cycle. The heart likewise has a basic rhythm, which is further modulated by neural and humoral factors.

At the meeting I was privileged to meet Professor Franz Halberg of Minnesota, the father of circadian rhythms. His work, and that of others, clearly has widespread applications in clinical medicine. Heart attacks, for instance, occur more frequently in the early hours of the morning, as does sudden death, for many possible reasons; also on Mondays, and also in the winter, because "the heart does not like the cold." Every serious student of hypertension knows that blood pressure tends to decline in the late afternoon and then rise again in the early morning, which clearly impacts on what drugs to use and when. In some secondary forms of hypertension, including toxemia of pregnancy, this diurnal variation is lost, as it also is in certain essential hypertensive "non-dippers," who may be at higher risk of developing end organ damage. Some patients in addition exhibit longer rhythms of blood pressure, some extending over days, complicating the very diagnosis of raised blood pressure.

Other diseases - such as nocturnal asthma - also exhibit a definite relation to time. Diurnal rhythms are common in endocrinology - indeed it was the observation that cortisol secretion exhibited its well known diurnal variation that first stimulated Professor Halberg's interest in this subject. There are circadian rhythms in pulse rate, blood pressure, body temperature, platelet aggregability, lymphocyte circulation, electrolyte excretion, and hormone secretion.

Progress in the study of rhythms may help improve the treatment of many conditions. We now understand that sleep is regulated by cells with intrinsic rhythmicity that are grouped together, especially in the suprachiasmatic nucleus of the hypothalamus. These cells retain their rhythmicity when transplanted into other areas of the brain and have innate rhythms of 22-25 hours. They receive afferent impulses from the photoreceptors of the retina, are "entrained" or synchronized by light to the 24 hour cycle, and send efferent messages via nerve tracts and through the blood stream. It is by no means an accident that melatonin, the hormone of darkness, is produced from the nearby pineal gland; and it is this effect of light and darkness that may account for the periodicity of certain reproductive functions such as menstruation. It is possible that in the near future many of these systems will be manipulated by drugs, light, or other means. This could provide new forms of treatment for sleep disorders, perhaps for affective disorders, and also for jet lag - thus allowing unencumbered travel to even bigger and better meetings on these topics.