Many physiological functions oscillate in a manner conducive to a regular pattern of existence, in which nocturnal rest alternates with diurnal activity. Urine flow is low at night when we hope that our sleep will not be interrupted by the discomfort of a full bladder. If we wake in the night we are not usually hungry, though many hours have elapsed since our last meal. We are in the main more wakeful and alert during the day than by night. Body temperature is higher by day, and there is some evidence that this contributes to mental efficiency. The adrenal cortex is most active in the morning, and cortisol secretion ceases for most of the night; in so far as cortisol plays a part in resistance to various stresses and strains that are seldom encountered by night, this timing is appropriate. There is now ample evidence that most or all of these rhythms persist in the absence of the numerous influences of habit and environment that might at first sight be considered causative. They are, therefore, described as endogenous, and, since they have a period around 24 hours, are termed circadian.

For anyone who departs from the usual pattern of diurnal activity and nocturnal rest, a persistence of the usual rhythm is no longer appropriate. The diurnal sleep of night workers, for example, is commonly interrupted by a full bladder. Such people, however, even if their hours of work are regular, depart from the usual pattern of work and leisure, meals and sleep, in many respects apart from a simple time shift. By contrast, the man who flies through several time zones is subjected to a sudden phase shift of all the rhythms around him: he must put his watch forward or back by some hours, and sunrise and sunset, hours of work and of meals, will all conform to this new time, except where the habits of his country of arrival differ from those of his country of departure.

It is now generally accepted that much of the discomfort arising from long flights is due to the resultant asynchrony between the persistent physiological rhythms and the new phasing of times for work, meals, sleep and so on. For example, records of actual sleeping habits of aircrew presented by Preston (1970) suggest that they have considerable difficulty in sleeping at a
time when it would not be night at home, even though they are tired and it is night where they are attempting to sleep; some of the altered sleep patterns recorded by Evans et al. (1972) after a flight from England to San Francisco also conform to expectation if the rhythm of sleepiness and wakefulness established in England had persisted.

One might suppose that with the frequency of air travel, observations upon the time course of adaptation of physiological rhythms after flight would abound. Unfortunately most of the variables that show a circadian rhythm are also affected by many other influences: urine flow is increased by free consumption of ethanol, wakefulness is prolonged by stimulating company or by an engrossing task, appetite can be stimulated by the cuisine, so that isolation of the rhythmic circadian influence demands a stringent control of conditions, which is usually unacceptable to those who travel for business or pleasure. Observations after real flights are, therefore, limited, both in numbers and in the range of data recorded.

It is well established that a long flight does not of itself cause any subsequent disturbance of circadian rhythms. This has been shown by northward or southward flights with minimal time-zone displacement (Hauty and Adams, 1966a; Gerritzen et al., 1969). Similarly, if a traveller crosses many time zones and returns promptly, his rhythms are almost undisturbed; this has been shown by Lafontaine et al. (1967a) for a flight from Paris to Anchorage and back, and by Gerritzen (1962) for a flight from Amsterdam to New York and back. By contrast, when travellers remain in the new zone for several days after a long flight, observed rhythms have taken several days to adapt to the new time. Among other components, this has been shown for temperature (Hauty and Adams, 1966b, c) and for urinary excretion of corticosteroids (Gerritzen et al., 1969; Wegmann et al., 1970; Haus et al., 1968; Halberg et al., 1969). Lafontaine et al. (1967b) measured corticosteroid excretion and, also, urinary sodium and potassium. Unlike most workers who have only recorded the mean of a group of subjects, they published the results for their two subjects separately. A clear difference between them emerges: on the fifth day in Anchorage both had fully adapted excretory rhythms for urinary potassium; in one, the excretory rhythm of 17-hydroxycorticosteroids was also fully adapted, but in the other this showed two maxima, corresponding roughly to the expected hours on Paris and on Anchorage time. On returning to Paris their steroid rhythms had completely failed to readapt to Paris time five days later, although the potassium excretory rhythm of one, but not of the other, had readapted.

Such apparent dissociations between different functions which normally oscillate with a regular phase relationship are of particular interest when one
searches for causal connections between different components; and such disassociations can most readily be sought if one measures a large number of variables which oscillate in a circadian rhythm. For this reason, as well as because of the difficulties in making sufficient observations before and after real flights, we (Elliott et al., 1972) have studied subjects exposed to simulated time-zone shifts. For this purpose we use an isolation chamber wherein four subjects can live for prolonged periods completely isolated from any indication of the alternation of day and night. They first spend several days there to develop a regular pattern of meals and other activities, and to provide data from which their circadian rhythms can be defined. If we are studying time-zone shifts we then enter the chamber and put the clock, usually eight hours, backwards or forwards, telling them to imagine they have now flown to San Francisco or Singapore, and to adhere strictly to their former pattern of living, following the new time indicated on the clock. At regular intervals they collect urine samples for subsequent analysis, measure body temperature, and perform an array of psychometric tests. Blood samples, for measurement of plasma phosphate and corticosteroids, are taken only on selected days to avoid too many venepunctures. More recently, we have measured temperature continuously during sleep by telemetry from a rectal probe.

Any study of rhythms generates a very large number of quantitative measurements and poses the problem of how best to summarise them without loss of useful information. One widely-used technique is to fit a sine curve by a conventional least-squares technique, and thus define the rhythmic component in terms of two parameters, amplitude and phase, if the period is assumed to be 24 hours. A simple statistic which emerges is the acrophase, or predicted time of maximum. Figures 1 and 2 show examples of experimental data with fitted sine curves which, at least on inspection, give a reasonable description of times of maximum and minimum; when, as in Fig. 2, the actual course of the variable departs far from a sine curve, the minimum is still accurately defined, and the maximum is defined as in the middle of the long plateau. By the criterion of movement of the acrophase, it appears that different subjects adapt more or less rapidly, as do different variables in the same subject. Figure 3 shows the time course of adaptation of the urinary potassium rhythm of two subjects after a simulated flight of eight hours eastward; although they were living together, one was largely adapted on the first day, while the other was hardly adapted at all even on the fifth day. Figure 4 shows the adaptation of urinary potassium and sodium rhythms in another subject after a similar simulated eastward flight; the sodium rhythm has adapted immediately but the potassium rhythm has been much slower. Figure 5 shows in yet another subject the sodium and potassium excretory
Fig. 1. Potassium excretion on thirty-seventh day after a flight from England to Chicago, with best-fitting sine curve (data of Elliott and Mills, 1969).

Fig. 2. Hourly performance upon a psychometric test to show symmetrical but non-sinusoidal rhythm, where the best-fitting sine curve specifies the maximum and minimum times appropriately, but fails to indicate the amplitude (Fort, A., and Mills, J. N., unpublished data).
rhythms on a control day, when they are nearly in phase, and on the first day after a simulated 8-hour westward shift; sodium has adapted immediately, potassium not at all, so they are now almost exactly out of phase with one another. Such observations suggest that factors controlling the sodium and potassium rhythms are different, and that the endogenous component in the sodium rhythm is overshadowed by some direct external influence.

Simpler indices of adaptation can sometimes be used, particularly when data cannot be fitted by a sine curve. Figure 6 shows the rate of nocturnal potassium excretion, expressed as a proportion of the 24-hour mean. Under control conditions this is usually around 0·5, but on the first or second day after a time shift, it often exceeds unity. A further point exemplified in this
figure is that adaptation, the return of this ratio to a low value, is not smoothly progressive. It may be worse on the second day than on the first (C2, C3) or it may improve and then deteriorate (B2). Further, it might be expected that adaptation would be easier on a homeward flight, or in a simulated experiment on returning to real time; there are, however, many instances, both in the literature and in our own observations, where the reverse has been seen.

It has thus far been presumed that adaptation consists simply in a shift of the timing of the rhythm, indicated by the movement of the acrophase. Sometimes, after a time-shift, rhythms disappear and the usually rhythmic variables behave in a completely irregular fashion until a new rhythm emerges. Two other forms of adaptation are theoretically possible: a change in amplitude, or the appearance of a double rhythm, with two peaks corresponding to the old and the new time. These could, of course, be combined.

A diminished amplitude has only been recorded at all commonly for plasma
concentration of corticosteroids, where it is said to persist for many weeks. Blood samples are seldom collected as frequently as would be desirable for a proper characterisation of these rhythms; and a minor change in timing, resulting in the collection of samples at a time further from the maximum, could easily give a spurious appearance of diminished amplitude. Figure 7 shows an example, from the data of Lafontaine et al. (1967b). Blood samples for corticosteroid analysis were collected on the day before leaving Paris, and on the fifth day after arrival in Anchorage. The phasing has clearly adapted to Anchorage time, but the amplitude appears low; this may well be due to the lack of a sample anywhere near to 09:00 hours by Anchorage time, when the highest concentration would be expected in an adapted subject.

Rhythms with two peaks are not uncommon, and cannot be analysed by conventional sine-fitting techniques. Another method of analysis, which does not depend upon the conformity of a rhythm to a sine wave or to any other specified form, is that of cross-correlation. Two days can here be compared, a control day and a day after time shift, and each value on the experimental day is correlated with the values on the control day at the same hour, one hour earlier, two hours earlier, and so on round the clock, the highest correlation
indicating that time shift which best fits the data. Figure 8 shows hourly measurements of potassium excretion before, and three days after, a simulated 8-hour westward time-zone shift;

![Graph of Hourly Excretion Rates of Potassium](image)

Fig. 8. Hourly excretion rates of potassium, plotted on real time for a control day, and on experimental time on the third day after a simulated 8-hour westward time-zone shift.

![Graph of Cross-Correlation](image)

Fig. 9. Cross-correlation between the curves of Fig. 8, with different time shifts. The maximum correlation at -3 hours suggests that the shift in the rhythm was still 3 hours short of the expected 8-hour shift.

8-hour westward time-zone shift; the data are obviously of similar but non-sinusoidal shape, and the cross-correlation coefficients shown in Fig. 9 suggest that the rhythm has shifted by five hours, falling three hours short of full adaptation. The most serious limitation of this technique is the large
number of evenly spaced measurements needed for any satisfactory definition. This cross-correlation technique can be modified to analyse rhythms with two peaks, even when the peaks do not coincide at all precisely with those to be expected on old and on new time; and we have some preliminary data suggesting that the commonest pattern is a combination of a rhythm following the new timing with one whose timing is partly adapted.

Asynchrony between the rhythms of the subject and those of his environment is not the only difficulty in adaptation. It may well be that asynchrony between different components of his own rhythm are of some functional importance; such asynchrony between sodium and potassium excretion has been seen in Fig. 5, and, though it is not easy to see any harmful consequence here, asynchrony between other components may be less innocuous. Other disturbances after flights are consequences of the customary flight schedules; for example, it is usual to fly westwards across the Atlantic by day, thus prolonging the day and leading to unusual fatigue by bedtime, whereas the eastward flight is usually by night, eliminating five or six hours of the usual sleeping time.

What does all this amount to in terms of the well-being of air travellers who cross several time zones rapidly? That people adapt erratically and some more readily than others, might well have been asserted as a simple fact of observation. Before we can make any useful contribution to assisting adaptation, it seems to me that two things are needed. Firstly, we need some means of measuring those aspects of psychology or physiology that cause the traveller concern; these include, most obviously, his mental alertness and ability to conduct successful discussions, whether academic, commercial, or political. Secondly, we need to know more about the possible mechanisms that intervene between a hypothetical clock in the brain and the functions that we hope to adjust. Then it can be decided, if the choice is available, whether it is better to reset the clock, or to adjust the level of the required function: amphetamine before the conference, barbiturates at bedtime.

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Against Pollution

‘Beware of pissing in draughts’ wrote Andrew Boorde (1490–1549). This was not genito-urinary advice but a plea for clean air. ‘There is is nothing, except poison, that doth corrupt the blood of man, as doth a corrupt and contagious air. The air cannot be too clean and pure: considering it doth close and compass us round about, and we do receive it in to us, and cannot be without it, for we live by it as the fish liveth by the water.’ Boorde wanted to eliminate the things that ‘doth infect, putrify, and corrupt the air, as the influence of sundry stars, and standing waters, stinking mists and marshes, carrion lying long above ground, much people in a small room lying uncleanly, and being filthy and sluttish.’ The house builder had to avoid all these things and to avoid sweeping the house when people were in it as ‘the dust doth putrify the air, making it dense’. He also had to beware the snuff of candles and the savour of apples. He was exhorted to ‘let the common house of easement be over some water, or else elongated from the house. And beware of emptying of piss pots, and pissing in chimneys, so that all evil and contagious airs may be expelled, and clean air kept unputrified.’