tion concerning the neurochemical basis of the differences, and, in view of evidence for an important role for central monoamine neurones in behavioural control, focus interest on genetic variations in mechanisms regulating monoamine turnover.

Recently Ciaranello, Lipsky and Axelrod (*Proc. natn. Acad. Sci. U.S.A.*, **71**, 3006; 1974) have reported that the concentrations of three adrenal catecholamine synthesising enzymes, tyrosine hydroxylase, dopamine-β-hydroxylase and phenylethanolamine N-methyl transferase, are twice as high in the adrenals of Balb/cJ mice as in those of the related inbred strain Balb/cN, and that heterozygous progeny are intermediate between their parents in the concentrations of these enzymes. Ciaranello *et al.* (*J. biol. Chem.*, **249**, 4528; 1974) examined the F_1, F_2 and backcross progeny of the mating between these sublines and concluded that single gene loci control the steady state concentrations of each enzyme. The correlation between the activities of these enzymes suggested either that the loci were linked structural genes or that a single regulatory gene locus controls the phenotypic expression of the three enzymes. Ciaranello *et al.* (*Proc. natn. Acad. Sci. U.S.A.*, **71**, 3006; 1974) also draw attention to differences between the two strains in fighting behaviour after a 2-week isolation period. In this case analysis of the F_2 mice suggested the behavioural differences were determined by a single gene with fighting recessive.

Such genetically determined behavioural differences could be coincidental, a cause, or a consequence, of the altered enzyme levels, but evidence for a relationship between aggressive behaviour and central catecholamines (Scheel-Krüger, Randrup, *Life Sci.*, **6**, 1389; 1967; Welch and Welch, *Commun. Behav. Biol.*, **3**, 125; 1969) may be relevant to the association. On the other hand much recent evidence supports the hypothesis that there is an association between central catecholamine-containing neurones and the mechanisms of reward (Crow, *Psychol. Med.*, **2**, 414; 1972; Ritter and Stein, *J. comp. Physiol. Psychol.*, **85**, 443; 1973). The question of whether unitary neurochemical mechanisms are associated with single dimensions in behaviour is one which increasingly will have to be approached.

On the opposite side of the coin is an accumulation of evidence for environmental influences on central catecholamine turnover (Thierry, Javoy, Glowinski and Kety, *J. Pharmac. exp. Ther.*, **163**, 163; 1968; Lewy and Seiden, *Science*, **175**, 454; 1972). Such findings may illuminate how genetic and environmental influences interact in the pathogenesis of the psychoses.

A plasmid dissected

from David Sherratt

A NUMBER of features has made the bacterial plasmid Col E1 an increasingly attractive DNA molecule for studies of genetic organisation, DNA replication and gene expression. Its small size of 4.2×10^6 daltons, sufficient to code for about seven average-sized proteins, makes it easy to isolate and handle in analytical studies and its replication can conveniently be studied both *in vivo* and in a soluble *in vitro* system. In addition, the Col E1 molecule has a single unique site for double strand cleavage by the sequence specific restriction endonuclease *eco*RI. This provides an invaluable positional reference for structural and replication studies of Col E1 and also provides an ideal tool for *in vitro* construction of hybrid DNA molecules containing DNA from either pro- or eukaryotes covalently linked to Col E1 (see for example Herschfield *et al.*, *Proc. natn. Acad. Sci. U.S.A.*, **71**, 3455–3459; 1974).

Localisation and analysis of specific regions of DNA (such as replication origins, strand interruptions, specific protein binding sites) by electron microscopy or other techniques requires some reference point. In linear molecules with unique ends such as bacteriophage T7, the ends provide reference points (with ambiguity unless the ends are distinguishable). But Col E1 and many other DNA molecules of interest are either circular or like phage T4 have non-unique ends. Various approaches have been used to provide visual markers in such molecules. Inman (*J. molec. Biol.*, **18**, 464–476; 1966) used mild denaturing conditions to visualise the AT-rich regions of phage lambda as 'loops' which occurred at fixed unique positions. This technique has been widely used, though it is inapplicable for many molecules as small as Col E1. Another approach has been to construct heteroduplexes *in vitro* between molecules differing by a deletion or addition of genetic material (see Sharp *et al.*, *J. molec. Biol.*, **71**, 471–497; 1972), though this technique is not easily applicable to analysis of replicating molecules. The use of sequence specific restriction nucleases such as *eco*RI to introduce double strand breaks at specific sites in DNA is a relatively simple technique and is being extensively used in the physical mapping of small DNA molecules.

Replicating Col E1 molecules have been isolated from exponentially growing *E. coli* cells, by Lovett, Katz and Helinski (*Nature*, **251**, 337–340; 1974), from *E. coli* minicells by Inselberg (*Proc. natn. Acad. Sci. U.S.A.*, **71**, 2256–2259; 1974) and from a soluble *in vitro* system which allows Col E1 initiation, semiconservative replication, termination and ligation to give complete closed circular duplexes (Tomizawa *et al.*, *Proc. natn. Acad. Sci. U.S.A.*, **71**, 802–806, 1403–1407, 2260–2264, 4935–4939; 1974). In each of these systems, the majority of replicating molecules when examined by electron microscopy are seen to be circular with two branch points; such *theta* structures are characteristic replicative intermediates of many circular replicons. The positions of the branch points with respect to the *eco*RI cleavage site were determined independ-

THE FATAL BALLOON ASCENT

THE readers of NATURE are no doubt aware of the fatal result of the recent ascent of the balloon *Zenith*; the following authentic details at first hand will no doubt be of interest:—

CIRON (Indre), April 17.

The *Zenith* was sent up on the 15th of April in order to determine the quantity of carbonic acid contained in the atmosphere at an altitude of 24,000 feet. The "let go" was given at twenty-five minutes to twelve A.M. The captain was M. Sivel, and there were only two passengers, M. Gaston Tissandier and M. Crocé-Spinelli. The ascent took place gradually in a slight E.N.E. wind, the sky being blue but vaporous. The rate of ascent was calculated to be nine feet per second, but diminished gradually. Shortly after one o'clock the altitude obtained was 22,800, and the passengers were quite well, although feeling weak. The inhalation of oxygen produced good restorative effects when tried. Then a consultation took place, and the *Zenith* being in equilibrium, a quantity of ballast was thrown overboard. M. Tissandier then fainted, and is ignorant of what was felt by his friends.

At eighteen minutes past two he was awakened by M. Crocé-Spinelli warning him to throw over ballast as the balloon was fast descending. He obeyed mechanically, and at the same time Crocé-Spinelli threw overboard the aspirator, weighing eighty pounds. Tissandier then wrote in his book a few disconnected words, and again fell asleep for about an hour. When he awoke, the balloon was descending at a terrific rate; no more ballast was left to be thrown away, and his two friends were suffocated. Their faces had turned black, and the blood was flowing from their mouth and nose. They were evidently dead. It was a terrible situation.

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