hara *et al.* remind the reader that, in the intact organism, the initial response to exogenous ET-1 is vasodilation[9]. They refer to work *in vitro* demonstrating that lower concentrations of the peptide cause endothelium-dependent relaxations because of the release of EDRF/NO. However, because inhibition of NO synthase caused comparable absolute increases in blood pressure in mice heterozygous for the ET-1 gene and in controls, Kurihara *et al.* conclude that a reduced release of NO does not explain the increase in arterial blood pressure seen when production of ET-1 is limited.

They are probably right, but only probably. The initial pressure was different in the two groups of mice, and it is difficult to compare the magnitude of vasoconstrictor responses in face of a changed baseline. For the same reason, further studies will be required, especially in the absence of proper concentration–response data, before one can fully accept their interpretation that the sensitivity of the endothelin receptors is the same in the two groups.

To come back to the issue of the reduction in endothelium-dependent effects of ET-1, as a contributor to the increased arterial pressure in mice heterozygous for the gene, one should keep in mind that endothelins not only cause release of NO but also that of other endothelium-derived vasodilators, such as prostacyclin and endothelium-derived hyperpolarizing factor (EDHF; ref. 13). To judge from experiments in rats, the release of EDHF by endothelin is more pronounced in young animals[13], and could contribute to a depressor effect of the peptide in the very young mice used by Kurihara *et al.*

Overall, however, the experiments with the ET-1 heterozygotes are not only notable for their elegance but also for the important general message inherent in them. They show the need to concentrate on the effects of small amounts of endothelins (which have a depressor and vasodilator action in the intact organism), before considering the vasoconstrictor effects (which probably come into play only when their production is grossly accentuated). Endothelin-1 may not differ from catecholamines, serotonin or even vasopressin, all of which can have profound vasodilator effects that are often forgotten because of the overwhelming vasoconstriction that they cause at higher concentrations.

But the most extraordinary finding of Kurihara *et al.* is that absence of ET-1 in the embryo results in major abnormalities of the pharyngeal arch, and in the inability to breathe. This is so unexpected that it is, as yet, hard to comment on. The causal link between the absence of the peptide and the malformations finds support from results *in vitro*, where exogenous ET-1 has a positive effect on embryonic development. Endothelins have been considered by some authors to stimulate cell growth (see ref. 11), but the new results promote ET-1 to the status of a key player in directing differentiation in a crucial (albeit localized) part of the body.

Moreover, the authors allude to the possible involvement of the peptide in the central-nervous control of breathing. Given accumulating evidence that the airway epithelium may be a major source of endothelin, we could be witnessing the emergence of endothelin as a general regulator of the formation and function of the respiratory system. In that regard, Kurihara *et al.* rightly note that their observations may provide a first glimmer of understanding of congenital anomalies such as Pierre–Robin and Treacher–Collins syndromes.

Finally, it seems that we also have the solution of a mystery — why nature has perpetuated the ability to produce a complex peptide such as endothelin, one which bears a strong resemblance to certain snake venoms and which is potentially so harmful if over-produced. Kurihara *et al.* now provide the answer: it is a matter of life and breath. □

Paul M. Vanhoutte is at the Institut de Recherches Internationales Servier, 6 place des Pléiades, 92415 Courbevoie Cedex, France.

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Corrections

■ The longest contiguous sequence of human DNA lodged in the data libraries is not the 73 kilobases of the β-globin region (News and Views, 3 March 1994; page 14). Rather that honour belongs to 180 kilobases encompassing the human retinoblastoma locus, deposited with GenBank by T. P. Dryja and colleagues (*Genomics* **17**, 535–543; 1993).

■ Discussion of the work of D. A. Maslov *et al.* (News and Views, 24 March 1994; page 288) should have also taken in a paper by L. F. Landweber and W. Gilbert that appeared in February (*Proc. natn. Acad. Sci. U.S.A.* **91**, 918–921; 1994). These authors also dealt with RNA editing in trypanosomatids, and came to broadly the same conclusions as Maslov *et al.*

DAEDALUS

Hidden motives

A PARASITE or disease organism lives by exploiting its host. A tapeworm steals your food, and an infection subverts your body chemistry. But they must do more than this: they have to propagate their kind onto further hosts. Accordingly, many parasites encourage their hosts to behave in ways that help the parasite to spread. Tuberculosis makes its victim cough and spit: this spreads the bacillus around, to be inhaled by other people. Hydrophobia goads a mad dog into biting other creatures, thus injecting them with the virus. A certain snail fluke causes the snail to climb grasses, so as to be more vulnerable to the birds that are the fluke's next host.

Musing on this principle, Daedalus began to wonder how deeply it influences human society. Perhaps compulsive hand-washing is triggered by an organism that is propagated on bars of soap. The custom of social kissing may be spread by an ingenious lip fungus. The bureaucracy that increasingly strangles whole societies may be an obsessive syndrome propagated by some malign organism that lurks in paper. It is clearly worthwhile to investigate just how, and how widely, parasites and disease organisms contrive to influence human behaviour.

So DREADCO's biochemists are studying various diseases which seem to modify the behaviour of their victims. Colds and influenza, for example, make the sufferer listless and unenterprising. The pathetic malaise invites others to crowd round with help and sympathy, and thus exposes them to the virus. The infection must release in the victim's bloodstream a sort of 'elixir of exhaustion'. Once identified and synthesized, it could prove a powerful antagonist to the obsessive drive of potential heart-attack victims, the hyperactivity of children and the fanaticism of zealots. A recent correspondent (D. F. Johnson *Nature* 368, 93; 1994) suggests the use of intestinal worms to counter eating disorders. Daedalus hopes to achieve this result at second hand, so to speak. He notes that some worms make their hosts grow faster. Presumably the worm, needing its host to eat enthusiastically, puts out some natural appetite stimulant. If isolated in pure form, this stimulant might boost the growth of sheep and cows, and even cure anorexia nervosa. Similarly, the organisms of venereal diseases should encourage their hosts to propagate them in the obvious way. This encouragement might also be chemical. Daedalus is culturing these organisms in search of that unholy grail, an effective, natural aphrodisiac. David Jones