smaller than that for silicate rocks. So the erosion rate for iron meteorites is about 22 μm per million years.

The authors investigated the possibility that the dust particle flux had varied as a function of time. Microcraters on lunar rocks indicate that the flux has remained constant within a factor of 2 for the last 20 million years. There is no information about the small particle flux before this time. As regards large craters, however, it can be concluded that the flux of objects responsible for craters with diameters between 0.01 and 100 km has remained constant to within a factor of 50 per cent for the last 850 million years. By comparing craters on Mars with those on the Moon the authors concluded that there has been no change for nearly 10^9 years in all regions of the Solar System between 1 and 4 AU from the Sun.

The discrepancy between the ^{40}K exposure ages and the ^{39}Ar, ^{10}Be and ^{36}Cl exposure ages could be explained if the erosion rate of iron meteorites was 200 μm per million years, but it has been found to be nine times less; or if the flux of small particles had increased, but it has been found to be constant for about the last 10^9 yr; or if meteorites had had the same collision history, but this is highly unlikely. So one is left with the conclusion that there has been a real change in the cosmic ray flux in the inner Solar System during the last 10^9 yr. And the meteorites indicate that the present flux, the one active over the last 10^6 yr, is about 45 per cent higher than the average flux over the previous 10^9 yr. The next problem, needless to say, is to find out why the cosmic ray flux changed. □

Prohormones for vasopressin

from B. T. Pickering

"STUDIES on the distribution and biosynthesis of neurophysin within the neurones of the [hypothalamo-neurohypophysial complex] suggest the interesting possibilities that either neurophysin and vasopressin share a common precursor or that there is a common genetic unit that controls the synthesis of the major components of the neurosecretory substance." Thus wrote Howard Sachs in 1969[1] and, during the past 12 years, more and more evidence has accumulated in favour of such a common precursor (see, for example, ref.2). The final vindication of Sachs's suggestion is reached today with the publication, by Richter and his colleagues, of the complete amino acid sequence of the bovine vasopressin-neurophysin precursor (see this issue of *Nature*, p.299).

This sequence, deduced from cDNA prepared from hypothalamic mRNA, reveals no surprises, being composed of a leader (or signal) peptide separated by a pair of basic residues from the sequence of arginine vasopressin which is followed by a glycyl residue and a further pair of basic amino acids and then the 97 residue sequence of bovine neurophysin II. The 17.3K precursor is completed with a carboxy-terminal 39 residue polypeptide which represents the glycopeptide known to coexist with vasopressin and neurophysin in the secretory granules of the neurohypophysis[3,4]. Such a sequence had already been predicted in several laboratories, both from isolation of putative precursors labelled *in vivo* and from the nature of the polypeptides synthesized in cell-free systems directed by hypothalamic mRNA. This is not to detract from the latest work of the Richter group, which has not only substantiated the size of the vasopressin precursor but established the order of the component polypeptides within the sequence. It will be interesting to see the nature of the carbohydrate side chain, the biological importance of which is unknown. Even more so because there is no evidence for such glycosylation of the oxytocin precursor which is considerably smaller than the vasopressin one. No doubt the Richter group will soon provide the cDNA, and hence the sequence, of this precursor too.

The successful elucidation of the nature of this vasopressin precursor, while concluding a chapter, does not end the story. As discussed in these columns last year[5], Paul Cohen and his group in Paris have drawn attention to the presence in bovine posterior pituitary extracts of much larger molecules (140K) containing the immunodeterminants of neurophysin and vasopressin and thus qualifying for consideration as putative precursors. This work has now been extended[6] and the 140K species has been shown to behave as one of 80K if examined under denaturing conditions. Moreover, this material appeared to consist of two components, linked by both a labile peptide bond and a disulphide linkage, which could be dissociated to give a 10K polypeptide that showed sequence homology with neurophysin and a 68K one which lacked the immunodeterminant for neurophysin. Rosenior *et al.*[7] also have evidence for immunoreactive vasopressin and neurophysin species of about 80K and 40K in rat hypothalamic extracts, and consider them to be putative precursors.

Arguments against such precursors come from the failure of extracted mRNA to direct the synthesis of products larger than 20–25K and, now, from the apparent completeness of this message with start and stop codons. The French group has argued that the 80K molecule might be directed by a different mRNA than the one preferentially extracted. However, in none of the *in vivo* studies has there been indications of incorporation of tracer amino acid into immunoreactive neurophysin or vasopressin species larger than 25K so that such a message would necessarily be present in minute amounts — much smaller than would be suggested from the relative proportions of larger vasopressin components found by Rosenior *et al.*

Very recently the 80K vasopressin/neurophysin putative precursor has taken on even more significance. Cohen and his colleagues have shown[8] that its 68K fragment contains immunoreactive sequences for both ACTH and β-endorphin, and that biologically active ACTH can be released from it by limited proteolysis. They interpret their data to suggest the existence of a pluripotent molecule which is a common precursor for all, or many, of the neuropeptides found in the posterior pituitary and which they term neurohypophysial coenophorin.

Quite apart from the rigorous criteria necessary to ascertain that large molecules, especially those rich in disulphides, do not arise from self-association of smaller ones (criteria which have been applied by Cohen and his associates), it should perhaps be questioned whether a large polypeptide containing within it the sequence of a smaller one is necessarily a precursor of the latter rather than vice versa. As part of the secretory process a newly synthesized polypeptide is packaged into secretory granules and, in every system which has been studied, there is evidence for a proportion of the secretory product being bound to the granule membrane. Could the large molecules discussed above represent such membrane-bound components which are in fact covalently linked to membrane proteins? Certainly a membrane-associated component from the ACTH system might share many of the properties of a similar component from the neurohypophysial system. Its presence in neurohypophysial extracts might arise from the close association of the pars intermedia and the pars nervosa in the pituitary gland.

Whatever their origin, these large molecules do present a fascinating problem, the solution of which will tell us much more about the nature of the secretory process in the polypeptide-producing cell. □

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1. Sachs *Adv. Enzym.* **32**, 327 (1969).
2. Russell *et al. Endocrinology* **107**, 1880 (1980).
3. Jones & Swann *J. Physiol., Lond.* **245**, 45P (1975).
4. Béguin *et al. J. biol. Chem.* **256**, 9289 (1981).
5. Pickering *Nature* **288**, 177 (1980).
6. Béguin *et al. J. biol. Chem.* **256**, 9289 (1981).
7. Rosenior *et al. Endocrinology* **109**, 1067 (1981).
8. Lauber *et al. Proc. natn. Acad. Sci. U.S.A.* **78**, 6086 (1981).

0028-0836/82/040280-01$01.00