NEWS AND VIEWS

Calcium Triggers Release of Packaged Secretions

THE mechanism by which neurotransmitters, hormones, histamine and other packaged secretions are released from cells is of great pharmacological importance. The release follows a specific stimulus, usually depolarisation or attachment of a chemical agonist to the plasma membrane. Evidence has accumulated that in many different systems coupling of stimulation and secretion requires the presence of calcium ions in the extracellular medium; Ba^{2+} or Sr^{2+} but not Mg^{2+} can substitute for Ca^{2+} . In certain situations, however, this requirement has not been demonstrable, and the role of Ca^{2+} in stimulation-secretion coupling has been doubted by some investigators. The possibility nevertheless remained that Ca^{2+} might be released from an intracellular store analogous to the sarcoplasmic reticulum of muscle. Such smooth membrane Ca^{2+} storage vesicles have a long evolutionary history, since they are present in slime moulds, and they may be widespread in animal cells. To resolve this problem, ways of measuring and controlling the concentrations of Ca^{2+} in the general cytoplasm, as opposed to vesicles, are required.

During the past few years, progress has been made in estimating cytoplasmic Ca^{2+} concentrations with the luminescent protein aequorin. These investigations have confirmed that there is an increase in Ca^{2+} in the cytoplasm after membrane depolarisation and preceding muscle contraction, and also in stimulated presynaptic nerve endings which are releasing neurotransmitters. Recently a calcium ionophore, A23187, which increases the permeability of membranes to Ca^{2+} , has become available; in the presence of the ionophore the concentration of Ca^{2+} in the cytoplasm can be varied by altering the concentration in the extracellular medium. Foreman and his colleagues (see page 249 of this issue of *Nature*) have made use of

the ionophore to analyse the role of Ca^{2+} in triggering the release of histamine from rat peritoneal mast cells. When peritoneal cells were exposed to A23187, $^{45}\text{Ca}^{2+}$ uptake was increased and histamine was released in proportion to the amount of Ca^{2+} in the extracellular medium in the same concentration range as required for release by antibody and antigen. In the presence of A23187, Sr^{2+} in the medium also released histamine.

These results suggest that an increase in cytoplasmic calcium concentration is the normal trigger for release of histamine and other pharmacologically active agents from mast cells. The subsequent events are still speculative. The interesting parallelism between the ions bringing about release of packaged secretions and those triggering the contraction of muscle has led to speculations that an actomyosin-contraction system in the peripheral cytoplasm participates in granule release. The dependence of the release on metabolic energy and its inhibition by cytochalasin are consistent with this possibility. Ca^{2+} is known to interfere with assembly of tubulin into microtubules, so it seems unlikely that assembly of microtubules is required for secretion. Coordinated action of microfilaments providing a motile force and microtubules providing guidance could, however, occur.

Since the concentration of Ca^{2+} in the cytoplasm may be an important regulator, not only of the actomyosin system, but also of other reactions such as the assembly and breakdown of microtubules in cell division and activation of certain enzymes, the discovery of an ionophore by which the concentration of calcium in the cytoplasm can be varied is likely to have many applications in cell biology.

From a Correspondent

When did Plates Start Breaking Up?

ONE of the central pillars of geology is the doctrine of uniformitarianism, which goes back to the 1830s and Lyell. The concept that geological processes have been of much the same intensity throughout the whole of geological time is very simple. There is wide consent on uniformitarianism and whatever controversy it raised in the nineteenth century, when catastrophism was its rival, it is taken for granted now. Which makes it fascinating when geologists suddenly find that they have been using it unthinkingly and perhaps mistakenly.

When plate tectonics was first proposed, it was clear that in some parts of the Earth continental plates are colliding with each other. Such a process is going on at present along a complicated belt of orogeny or mountain building from the Alps to the Himalayas. Since today separate continental fragments can be seen being welded together, the natural reaction is to suppose that similar plate tectonics concepts have always applied and that continents as they are at present have been put together by a steady process of mosaic building. Of course, the

process is not entirely one of building because there are break-up processes—rift formation—going on simultaneously. The question is whether these activities have been going on since the beginning of geological time and obviously the complexity of unravelling the past gets greater the further back one tries to go.

Piper, Briden and Lomax in this issue of *Nature* (page 244) find a neat way to answer the question without having to do any of the unravelling. The Precambrian area of Africa has a pattern of stable blocks between which are orogenic belts. These belts, on a plate tectonic interpretation, are ancient convergent zones—"Precambrian Himalayas". There are, however, some geological reasons to doubt this explanation and to suggest that the belts are ensialic—that is, that they have their origins in continental rocks.

Piper *et al.* test these hypotheses by using palaeomagnetic data. They construct polar wander paths for the blocks separately and show that in the Precambrian the poles for the separate blocks follow rather similar