The Organisation of Vomiting as a Protective Reflex:
A commentary on the first day's discussions

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Introduction

This symposium has shown that although there is a wealth of information available concerning the nature of vomiting, no consensus yet exists concerning the detailed mechanisms of the initiation and control of most clinically relevant forms of vomiting. There remain fundamental gaps in our knowledge and the symposium has played a valuable role in identifying and highlighting them. Further, it became evident during the course of the discussion periods that there were several themes or concepts in particular upon which it would be worth focussing further study and which could lead to valuable new insights.

This chapter explores those foci which were identified as a result of both the invited presentations and the contributions from the floor. It arose from an editorial decision to give an overview of each day's proceedings and an expressed desire on the part of a number of participants for us to go beyond a straightforward report of the discussion alone. We have tried to set the points in context by providing background data and some additional ideas concerning their possible significance. Those of us who met together to talk for two further days following the meeting in order to attempt this synthesis, hope that this discussion will help to point the way to future experiments and clinical trials which will further our knowledge of the underlying mechanisms of nausea and vomiting.

Key Issues

Some major and as yet unanswered questions which are central to the whole problem of vomiting have been emphasised as a result of the symposium:

1. What is the function of vomiting, particularly in man?
2. What are the relevant features of a vomiting stimulus?
3. What are the sites for the reception of vomiting stimuli and does the area postrema play more than a chemoreceptive role?

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4. What structural features of the area postrema are important to its' function?
5. How are the various responses involved in nausea and vomiting integrated within the central nervous system?

These questions are addressed below and where possible answers proposed on the basis of the data presented and the concepts discussed during the symposium. Ultimately, solutions to these questions will hopefully facilitate the design of more specific and effective anti-emetic drugs, and help alleviate this most distressing symptom and ubiquitous medical problem.

**Why Does Man Vomit?: An Hypothesis Involving the Hierarchical Organisation of a Toxin Defence System**

There are several mechanisms by which an animal may protect its body, and most importantly the CNS, from damage by ingested toxins. These may be placed in order of temporal effectiveness, the most immediately effective coming first:

1. The smell or taste of potential foodstuffs which may be avoided due to innate or learned behaviour
2. The detection of toxins by receptors in the gut followed by a central reflex producing an appropriate response; nausea to prevent further consumption, inhibition of gastric motility to confine the toxin to the stomach, and, if necessary, vomiting to purge the system of the already ingested (but not necessarily yet absorbed) toxin
3. The placing of a sensor located within the CNS to detect circulating toxins. This would provide a vomiting signal probably followed by central integration ultimately leading to vomiting.

An hierarchical arrangement (see Table 1) emerges from a consideration of this system which is based on data presented and discussed during the symposium. It may be seen that this goes some way to explain the disparate responses of different species to similar stimuli and perhaps similar responses of individuals to different stimuli. For instance, it is generally accepted that laboratory rats do not vomit; they do, however, develop a profound conditioned taste aversion (CTA) to wide-ranging stimuli (including X-irradiation and toxins) which actually cause vomiting in other species (Coil and Norgren 1981). (CTA is mediated as we know by the AP, the most likely candidate for the central receptor.) The omnivorous rat displays a bias, probably established by natural selection, to associate gustatory and olfactory cues with internal malaise even when these stimuli are separated by long time periods (Garcia et al. 1966; Rozin and Kelat 1971). The first line of defence in the rat (i.e. smell, taste) appears to be extremely highly developed (Roper 1984) and, therefore, perhaps as a result the third and last line has become redundant and is non-functional. In laboratory rats, even the second line of defence seems to be obsolescent because although it is known that gastric afferents in the rat respond to intragastric copper sulphate (Clarke and Davison 1978), vomiting does not result. The detection apparatus is still present, but the vomiting response is absent. Essentially, here we have an example where the primary defence mechanism is so highly tuned that the animal no longer needs to