disappointed with a radical approach and now palliate initially and aim to correct at about the age of 5 years. If early correction is contemplated in certain conditions in which palliation is not so helpful, not only must the anatomical diagnosis be exact, but the patients must be in as good a clinical state as possible preoperatively. In this respect, early referral of these sick infants and careful maintenance of the acid base state are vital.

CONCLUSION

We have attempted to record the performance of a regional unit dealing with a full range of cardiac disease. Full back-up is necessary from biochemical, haematological, and radiological services, from the physiotherapy department, and from the blood bank, but the organisation of the unit is simple and does not need much technical support. The unit does not use large amounts of homologous blood.

Although this study was not designed to show long-term results, our own experience is confirming the results of others that the obvious early benefit is sustained in most patients as time goes on.

Necessarily the cost per patient is high when compared with simpler surgical procedures but it is probably fairer to compare the expense we incur with the overall cost of treating other life-threatening or disabling diseases if such comparisons have to be made. In terms of symptomatic relief, return to a useful and productive life, decreased dependence on others, and, in children, the improved prospects for the future, including normality at school, we believe that we are showing that the expense is justified and is a sound and proper use of resources.

We thank the members of the junior medical staff, nursing staff, technicians, laboratory staff, and many others who have contributed so much to the running of this unit during the period covered by this report.

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Today's Treatment

Diseases of the alimentary system

Nausea and vomiting

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Complex processes underly the symptoms of nausea and vomiting. Presumably these mechanisms evolved to the organism's advantage. Boyle observed three centuries ago that "tis profitable for man that his stomach should nauseate and reject things that have a loathsome taste or smell."[1] Nevertheless, though the stomach may sometimes empty itself of certain noxious substances when this is required, nausea and vomiting often seem to serve no discernibly useful function. Seasickness, the commonest form of motion sickness, may be considered as an example. Its importance is emphasised by the fact that the word nausea is derived from the Greek for a ship. Analysis of the sufferer's symptoms and signs conveys a picture of complex autonomic changes. Pallor, coldness, sweating, salivation, nausea, and anorexia precede vomiting. In addition, there may be drowsiness, headache, and lassitude. It is impossible to conceive any advantage for the sufferer once he has embarked from the security of terra firma; and the imagination is stretched to impute a teleologically protective role to seasickness as a means of curbing exploratory and adventurous instincts.

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To treat the symptoms of nausea and vomiting rationally, a comprehensive diagnosis should have been established; the susceptibility and circumstances of the individual assessed; and possible hazards and disadvantages of symptomatic approaches considered. There are many conditions in which symptomatic treatment is not appropriate—for instance, nausea and vomiting are common accompaniments of abdominal disorders needing surgical treatment; or vomiting, sometimes without nausea, may be a feature of raised intracranial pressure. Similarly, when the symptoms are derived from metabolic or drug-induced disturbances, treatment of the underlying abnormality or withdrawal of a drug, rather than symptomatic measures, is needed.

Vomiting, particularly when forceful and accompanied by strain and retching, may itself have harmful consequences. The eponymous Mallory-Weiss and Boerhaave syndromes represent the most dramatic results of violent vomiting. Longitudinally placed laceration in the lower oesophagus, with resulting haemorrhage, occurs in the Mallory-Weiss syndrome, typically in someone who has had an alcoholic binge. But indulgence in alcohol is not a prerequisite for such lesions, which sometimes occur after strenuous vomiting for other reasons; patients with small sliding hiatus hernias are susceptible. Boerhaave's syndrome is an extremely rare catastrophe in which violent vomiting causes rupture of the oesophagus.

There are more prosaic but much more common consequences of vomiting. After abdominal surgery undue vomiting may interrupt recovery by delaying or preventing wound healing; or

after surgery sudden movement and changes in pressure may lead to vitreous loss. More generally, prolonged vomiting from whatever cause inevitably results in fluid and electrolyte loss, and among various consequences such depletion is then likely to perpetuate the symptoms of nausea and vomiting.

Centres and pathways concerned with vomiting

Drugs that suppress or modify the symptoms of nausea and vomiting act at various sites; these may be discussed in terms of neurological pathways and centres, so far as they are understood. Firstly, psychological stimuli to nausea and vomiting may be initiated by sights, smells, or associations perculiar to the person, and these are subserved by cortical pathways. Secondly, reflex stimuli operate from abdominal organs via both vagal and sympathetic afferent nerves. Thirdly, impulses originating from the vestibular organs are the primary cause of motion sickness. Fourthly, there are many compounds such as apomorphine, morphine, ergot derivatives, digitalis glycosides, nitrogen mustards, and probably numerous metabolites, that produce their effects humorally, acting directly on areas in the medulla.

The vomiting centre is in the reticular core of the medulla; its function is now thought to be one of co-ordinating various components in the act of vomiting. Many other centres exist close to the vomiting centre. They include a spasmodic respiratory centre, inspiratory and expiratory centres, vasomotor centre, salivatory nuclei, and bulbofacilitatory and inhibitory systems. The process of vomiting may need action by all these centres under the co-ordinating influence of the vomiting centre. On the medullary surface next to the vomiting centre is a second area known as the chemoreceptor trigger zone that responds to various compounds and transmits impulses to the vomiting centre. Many stimuli to vomit are transmitted directly from visceral organs to the vomiting centre and are independent of the chemoreceptor trigger zone. Vagal fibres are usually considered to be more important than sympathetic pathways; they, for instance, conduct impulses that start vomiting in patients with abdominal distension.

The actions of various emetics have been studied and illustrate the variety and complexity of possible effects. As an example, copper sulphate given by mouth in small quantities provokes impulses from receptors in the stomach that are then conveyed to the vomiting centre via both sympathetic and vagal fibres. In larger amounts copper sulphate when absorbed imposes a central action by directly stimulating the chemoreceptor zone. In other instances long-held assumptions have been challenged—for example, staphylococcal enterotoxin was thought to induce vomiting mainly by central actions, whereas its effect is now known to be primarily peripheral, on the gut.

Individual susceptibility

Wide differences exist between individuals' susceptibility to conditions that cause nausea and vomiting. Most people are seasick in rough conditions, but they acquire tolerance within a few days and then lose their symptoms completely. A few fortunate people are never affected and, at the other extreme, some remain highly susceptible. Another variation in vulnerability is that after surgical operations. "Postanaesthetic vomiting" occurs more commonly in women than men, is more likely after long operations, and decreases in frequency with advancing age.

The threshold of response of the chemoreceptor trigger zone is thought to be influenced by blood levels of certain hormones. Raised levels of oestrogen are considered to play a part in sickness of pregnancy, and in those who develop nausea when they first take oral contraceptives. Synthetic oestrogen given, for instance, in the treatment of prostatic carcinoma may cause similar symptoms. Greater understanding of the basis for differences in susceptibility to vomiting between the sexes and in different groups of people may lead to more effective therapeutic approaches. At present, however, the important practical implication of such differences lies in the special attention needed by those who are particularly vulnerable. In such people there is justification for prophylactic treatment and, if necessary, they may have to avoid anything particularly likely to induce sickness.

Antiemetic drugs

Four categories of drugs are valuable in the symptomatic alleviation or prevention of nausea and vomiting: anticholinergic drugs, antihistamines, derivatives of phenothiazine, and an orthopramide drug, metoclopramide. The actions of these drugs are seldom confined to one site; but atropine-like substances and certain antihistaminic substances act mainly on the vomiting centre, whereas the phenothiazines primarily influence the chemoreceptor trigger zone.

Hyoscine

Anticholinergic drugs have long been known for their antiemetic effects particularly in preventing or relieving motion sickness. In trials during the second world war hyoscine hydrobromide proved the most effective. Hyoscine has atropine-like actions, but it is also a central nervous depressant. In benefiting motion sickness the anticholinerigc action by which it blocks afferent impulses at the vomiting centre is important, but its cortical effects and also probably some peripheral influence on the labyrinth also contribute to its effectiveness. In therapeutic doses (0·6-0·9 mg) side effects are likely to include some drowsiness, slight headache, dryness of the mouth, and inability to read small print. The susceptible traveller usually considers these effects a small price to pay for the prevention of motion sickness. But caution is required in the elderly, in whom transient mental confusion may occur. A child under 5 years old may need 0·15 mg before travelling, though young children are, in fact, often less susceptible than their parents to the effects of motion. Children from 5-15 may need adult doses, but half doses are usually sufficient.

Antihistamines

The discovery that an antihistamine drug had antiemetic effects provides an interesting example of serendipity. Dimenhydrinate (Dramamine) was sent for clinical trial to the allergy clinic of the Johns Hopkins Hospital. During treatment with this drug a patient with urticaria noticed that she no longer suffered from car sickness. Dimenhydrinate was then given to USA troops crossing the Atlantic in the *General Ballou*, a rather top-heavy converted freight ship. Though it was found to be valuable in preventing seasickness, initial impressions were over-enthusiastic, and later trials failed to show any striking superiority over other remedies—particularly hyoscine.

Dimenhydrinate was thus established as the first antihistaminic drug shown to have antiemetic properties. Such properties are not common to all antihistamine preparations; the activity is specific, mainly by direct sedation of the vomiting centre, and is independent of the other actions of the drugs concerned. There is no direct correlation between the central effects of particular antihistaminic preparations and their potency as peripheral histamine antagonists. The antihistamine drugs that help motion sickness are also of some value in treating the nausea and vomiting caused by labyrinthine disturbances such as labyrinthitis and fenestration operations. The vomiting produced by apomorphine is scarcely affected, as the chemoreceptor trigger zone is not suppressed by these drugs. Examples of antihistamine drugs with antiemetic activity include: dimenhydrinate (Dramamine), cyclizine hydrochloride (Valoid), promethazine hydrochloride (Phenergan), and meclozine hydrochloride (Ancolan), the latter two being longer-acting than the former. The antihistamine drugs often induce drowsiness and unsteadiness that are enhanced by alcohol.

Phenothiazines

Those phenothiazine derivatives that possess antiemetic activity act primarily in blocking the chemoreceptor trigger zone. They exert general sedative effects as well, but there is little impact on the vomiting centre. This accounts for the fact that though impulses pass through the chemoreceptor trigger zone en route from the vestibular

organs to the vomiting centre, phenothiazine derivatives have not proved particularly useful in treating motion sickness.

Chlorpromazine in relatively low and non-sedative doses was found to prevent vomiting that would otherwise be induced by agents acting on the chemoreceptor trigger zone. This prompt and specific action is exerted either by competition for the receptor site or by a directly depressive effect on this area in the medulla. This potent and selective action has many useful clinical applications in conditions such as uraemia, carcinomatosis, radiation sickness, and in helping to counteract the nauseating effects of many drugs.

There has been no convincing demonstration of a greater antiemetic efficacy of one phenothiazine congener over another, but chlorpromazine is regarded as less suitable than some newer compounds because of the greater risk of jaundice. Advantages of the newer compounds are partly offset by a greater likelihood of inducing extrapyramidal effects. Examples of piperazine side-chain phenothiazines that have potent antiemetic activity include perphenazine (Fentazin), prochlorperazine (Stemetil), and thiethylperazine maleate (Torecan). The extrapyramidal side effects shown by oculogyric crises and muscle rigidity may render these drugs unsuitable for repeated administration in some patients.

Metoclopramide

Metoclopramide is a drug with unique actions in the upper gastrointestinal tract. It was synthesised in France from a derivative of procaine and then applied clinically in conditions associated with dysfunction in the gastroduodenojejunal area. Studies in many parts of the world subsequently confirmed that it possessed powerful antiemetic properties with an order of activity similar to the phenothiazines. In man it causes a rise in pressure at the lower oesophageal sphincter, increases both the frequency and amplitude of gastric contractions, and speeds the rate of transit through the small bowel. In patients with duodenal ulcers it accelerates gastric emptying, both of liquids and of isotope mixed with solid food. These actions render it pharmacologically distinct from other compounds in therapeutic use.

Other recent clinical studies on particular groups of patients who are apt to vomit owing to gastric retention are relevant. For instance, metoclopramide has been reported to improve delayed gastric emptying in diabetics. It also benefits gastric retention after gastric surgery. Observations on patients who have had antrectomies are relevant. One suggestion had been that a major action of metoclopramide in accelerating gastric emptying was by increasing the closeness of synchronisation between antral and duodenal contractions. Its efficacy in patients in whom the antrum had been removed indicates that it cannot solely act in that way. In fact, the mechanisms of its action remain poorly understood and debate continues even whether its effect is mediated mainly through nerves or directly on muscle. Studies in animals have also indicated some action on the chemoreceptor trigger zone, but undoubtedly the clinically important actions in man are on the motility of the upper gastrointestinal tract. Its limited central action is illustrated by its relative ineffectiveness in motion sickness. Metoclopramide does not cause frequent side effects, but lassitude and drowsiness sometimes occur when the drug is given in therapeutic doses, and occasionally extrapyramidal reactions are seen. In the adult such reactions are usually a consequence of taking too much of the drug.

Therapeutic approaches

MOTION SICKNESS

In both the prevention and treatment of motion sickness, when exposure is likely to last only a few hours, hyoscine hydrobromide is the most satisfactory drug (tab hyoscine *BP* 0·3 mg). Two tablets (0·6 mg) should be taken an hour before exposure to the motion and thereafter 0·3 mg may be taken at six-hourly intervals. Doubling the dose is more effective but other consequences, notably dryness of the mouth and drowsiness, are more evident. In prolonged exposure an antihistaminic drug, such as diphenhydramine 50 mg three times a day, or meclozine 50 mg once or twice daily, is preferred, with an expected 50-60% success rate. Such drugs may be continued for several days while tolerance to the motion is acquired. In some people who do not have responsibilities while travelling the sedative effects of cyclizine are desirable, in a dose up to 50 mg three times a day. Alcohol should be avoided while taking either hyoscine or an antihistamine preparation.

In the poor sailor both physical and psychological factors are relevant. Many people find their own remedies: they learn to avoid overindulgence in food and alcohol, shun stuffy cabins and nauseating smells, and avoid the company of those already afflicted. By remaining amidships they are less likely to be affected, and some rely on fixing their gaze on the horizon as a means of maintaining a stable posture.

NAUSEA AND VOMITING OF PREGNANCY

An important physical basis for pregnancy sickness may exist in alterations in levels of hormones, but the use of neither hormonal nor antihormonal agents is at present feasible. In current concepts of management special emphasis is placed on the application of conventional general measures. These include encouragement and psychological support, and the correction of nutritional and electrolyte imbalance. The doctor must ensure that the patient is taking frequent small meals rich in carbohydrate, and that her fluid intake is adequate. Ideally no drugs should be given during the first trimester. There are, however, occasions when a pregnant woman is so nauseated and anorexic that an antihistamine preparation or phenothiazine derivative is considered justifiable. Features such as weight loss, dehydration, or the restriction of normal activities provide a mandate for using such drugs. No well-controlled trial has shown one agent to be more effective than another.

When drug treatment is deemed essential it is usual to start with an antihistamine such as meclozine, promethazine, or trimethobenzamide, whereas those with severe nausea and vomiting and those who do not respond are given one of the newer piperazine side-chain phenothiazines. Chlorpromazine is considered less suitable than the newer compounds because of the slightly greater risk of inducing jaundice; but if there is associated epilepsy or suspected eclampsia the newer phenothiazine congeners are best avoided because of their tendency to produce extrapyramidal effects.

In patients with severe vomiting of pregnancy physical and psychological influences are difficult to separate. In addition, in any one person there is a small possibility that a disorder unconnected with the pregnancy may be contributing to the illness. The occasional presence of a disturbance such as raised intracranial pressure, peptic ulceration, hepatitis, drug reactions, and cholecystitis is easily overlooked.

POSTOPERATIVE NAUSEA AND VOMITING

The decrease in incidence of postanaesthetic nausea and vomiting has been attributed to the use of new anaesthetics, greater attention to efficient ventilation and hydration, and a greater awareness of the part played by opiate drugs used in premedication. In ill patients undergoing major surgery there may be dangerous side effects from some antiemetic drugs, especially hypotension. Routine prophylactic treatment with antiemetics is not indicated. In addition, opiates given postoperatively for pain, rather than included in the premedication regimen, cause less nausea and vomiting.

When antiemetic treatment is needed postoperatively three choices in drug treatment are available: (*a*) the antihistaminic drugs such as cyclizine and promethazine are only moderately effective but have the advantage of relative non-toxicity; (*b*) the piperazine side-chain phenothiazines, such as perphenazine and prochlorperazine are more potent but cause more side effects, with drowsiness, hypotension, and extrapyramidal symptoms liable to complicate the postoperative condition; and (*c*) metoclopramide is helpful in some patients and in the adult carries little risk of side effects. Metoclopramide is particularly valuable in reducing the risk of vomiting preoperatively or during induction of anaesthesia—for instance, for surgery in the casualty department or for a patient in labour.

TOXIC AND DRUG-INDUCED NAUSEA AND VOMITING

Nausea and vomiting in patients undergoing treatment for neoplastic diseases may be related in part to the underlying illness, but often the treatment is solely responsible. Virtually all patients given nitrogen mustard preparations have nausea, and about half of these will be subject to severe vomiting, which begins one to three hours after treatment. Cyclizine and promethazine provide partial control of the nausea and vomiting that follow treatment with cytotoxic drugs, but many patients are more effectively relieved by the more potent phenothiazine derivatives. Prophylactic administration given just before the cytotoxic agent is usually desirable.

MISCELLANEOUS CAUSES

Acute vomiting and diarrhoea caused by various pathogens, many of which are assumed to be viral, constitute one of the commonest diseases in the community. Antiemetic drugs are not of value in the symptomatic control of gastroenteritis. Cyclizine, however, has a place in controlling the persistent nausea which is often such an unpleasant accompaniment of hepatitis.

Several ototoxic agents including streptomycin affect the vestibular apparatus giving rise to vertigo, nausea, and vomiting; inner ear disease including Menière's disease, neuronitis, postural vertigo, and eighth-nerve tumours may have similar effects. Destructive middle ear disease and surgical procedures on the middle ear may also damage the inner ear and result in a symptom complex in which vertigo is dominant and which is accompanied by nausea. Dizziness and nausea may be helped by antihistamine drugs such as dimenhydrinate, cyclizine, or meclozine.

Patients suffering from Menière's disease causing frequent attacks may benefit from betahistine. This histamine analogue was developed because the parenteral use of histamine reduces the symptoms of vertigo and tinnitus in Menière's disease. Betahistine probably exerts its effect by reducing endolymphatic pressure. Antihistamines should not be used concurrently. Symptoms of nausea and headaches, as well as exacerbation of peptic ulceration, have occasionally been reported in patients receiving betahistine.

New surgical procedures are being devised to combat inner ear disease and may have to be considered in patients suffering from severe vertigo, nausea, and vomiting of inner ear origin. In some such patients the repeated administration of antiemetic drugs, including new phenothiazine derivatives, is justified even when there is the risk of causing extrapyramidal side effects.

Conclusions

Ryle observed that "symptoms are a part of morbid physiology; they express disturbances of function. As a rule, therefore, they precede the development of signs which are but the outward morbid anatomy of the living." He chose nausea as one of three symptoms to illustrate his thesis. Since the publication of his *Natural History of Disease*, the opportunities and expectations of symptomatic treatment of nausea and vomiting have greatly increased. There should be a concomitant increase in diagnostic precision if the doctor is to avoid inappropriate application of symptomatic drugs. In addition, it is evident that the sites and modes of action of antiemetic drugs are incompletely understood and that their side effects are often unpleasant and occasionally dangerous.

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Bone and Joint Diseases

Ligamentous injuries around the knee

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Though they are rare in children, injuries to the ligamentous structures of the knee joint are common after adolescence. The most common cause is a sports injury but they are seen after road accidents or any type of fall. When they are severe they may permanently alter the life pattern of young, physically active individuals—particularly their spare-time activities.

The ligaments of the joint are the static stabilisers. They surround the joint. They are strong at the sides and posteriorly, and the cruciate ligaments cross near the central pivot point. Anteriorly the ligaments are weak but this area is largely filled by one of the dynamic stabilisers, the extensor apparatus. Under stress, ligaments control stability when muscles, the dynamic stabilisers, are relaxed or strained to their limit.

The problems of knee ligament injuries are not appreciated by the sportsman. Commonly he will sigh with relief when a ligament damage is diagnosed in the belief that a semilunar cartilage injury, which he fears, is more serious. It is much easier to get a man back to a full active life by surgical treatment of a torn meniscus than after a serious ligament injury.

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Normal knee

The normal knee is stable in full extension. The stability is due to the fit of the femoral and tibial condyles and to the tautness of the medial and lateral ligaments and the posterior capsule. In this position there is no side to side or rotatory movement possible. Body weight is transmitted in front of the centre of the joint. The extensor muscles are relaxed.