Observations on the Etiology of Seasickness, with Special Reference to Cardio-Vascular Changes, and Indications for Treatment: : : : : : : : : :

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Thesis submitted for the Degree of M.D.,

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#### INTRODUCTORY.

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In the history of human ills seasickness is of immemorial lineage. For centuries it has been a subject of study obscured by unverified speculation and false analogy. An insuperable difficulty inherent in the problem is that it does not lend itself to controlled experimental observation and conclusive proof. Therefore no study of seasickness can be complete without some clear conception of its mode of origin. In the attempt to achieve some separation of fact from fancy, three fundamental axioms, based upon universally accepted observations, must first be postulated.

1. Excluding cases of sheer suggestion, which do not properly pertain to this subject, MOVEMENT OF THE SHIP IS A CONSTANT ANTECEDENT FACTOR. Symptoms increase up to a point as movement becomes more pronounced; diminish as movement becomes less; and nearly always vanish at the end of the voyage.

2. Whatever may be their source of origin or mode of action, THE DISTURBING STIMULI FINALLY RESULT IN A FUNCTIONAL DERANGEMENT OF THE AUTONOMIC NERVOUS SYSTEM.

3. Many sufferers find that their symptoms tend to abate after a certain lapse of time, even if there be no lessening of the movement of the ship. This shows that A PROCESS OF ADAPTATION OCCURS. Further proof of adaptation is the diminishing tendency to seasickness exhibited by the majority of people on successive voyages. Immunity thus acquired is in many at first only special to the ship in which it develops; later it may or may not become general.

Depending upon these three groups of facts, the subject thus divides itself naturally under three headings:-I. THE IMMEDIATE EFFECTS OF MOVEMENT; II. THE FINAL RESULTS; and III. THE ESTABLISHMENT OF IMMUNITY.

#### I. THE IMMEDIATE EFFECTS OF MOVEMENT.

The disturbing movement of a ship differs in four important respects from movements to which the body is normally habituated:-

1. It is of moderately short range, with sudden acceleration and retardation.

2. Its direction is almost always in more than one plane, being seldom purely vertical and never wholly horizontal.

3. It is continually varying in direction, often unexpectedly.

4. Its variations are usually irregular in rhythm and extent.

## (a) Predisposing Factors.

Certain preceding conditions affect both mind and body in such a way as to prepare an easy path for the disquieting effects of movement. (i) <u>Psychological</u>. The stolid, unaffected individual, whose mental vision is apt to be as limited as his reflex responses, is fond of saying contemptuously that seasickness is "all a matter of nerves." It is beyond question that previous personal experience of seasickness undermines selfconfidence to such an extent that sometimes the recollection alone will induce malaise. Even without this past experience, many impressionable people embark on a voyage with feelings of apprehension. One concept acquired very early in life is the dread alliterative association between "sea" and "sickness." Ever since the ancient Greeks spoke of <u>naus</u>, a ship, and <u>nausea</u>, sickness, the two words have been inseparably linked together.

(ii) <u>Physiological</u>. Granted the assumption that the phenomena of seasickness occur as a result of reflex activity of some part or parts of the nervous system, predisposing physiological factors may be presumed to consist of one or more of the following:-

1. Increased susceptibility of the nervous system to afferent stimuli initiated by the movements of the ship.

2. Increased activity of the cerebrospinal paths linking the afferent side of the reflex arc with the efferent.

3. Increased excitability of the efferent nerve-fibres and/or their effector organs.

4. Impairment of the normal cerebral inhibitory influence. (Most seasick patients have the knee-jerk and abdominal and pharyngeal reflexes highly active, although usually muscle-tone is diminished rather than otherwise).

Any or all of these aberrations may result from fatigue or past or present illness. Experienced travellers, previously immune, have occasionally reported their first attack of seasickness following a fatiguing train-journey, stress, excitement, or lack of sleep from various causes. All conditions augmenting the excitability of any part of the reflex arc will lower the threshold to subliminal stimuli. This is considered in more detail later.

## (b) Effects on the Erect Subject.

Reasoning <u>a priori</u>, one may expect that the movements of a ship at sea will cause, in those who are up and going about, excessive stimulation of the neuro-muscular mechanism responsible for the maintenance of equilibrium. This is initiated by:-

(1) Increase of afferent stimuli in number, intensity, or duration; or

(2) Alteration in character of stimuli; e.g. overstimulation of utricles and posterior and superior semicircular canals, which are set in action only by the vertical component of the ship's movement. In consequence of (1) or (2) or both, there ensues:-

(3) Augmented activity of reflex arcs. Pavlov's observation that stimulation of nerve-cells at one point in the brain leads to inhibition of adjacent parts, makes it seem probable that in a moving ship inhibition of contiguous centres may follow excitation of the cerebro-spinal centres involved in standing and in walking. These centres involve, directly or indirectly, almost the whole brain, and include the following:-

(i) The centres concerned in myotatic reflexes originating in "anti-gravity" muscles such as those of the neck and back, quadriceps femoris, and gastrocnemius. These centres comprise (a) the central terminations of the antero-lateral tract in the medulla and cerebellum; and (b) the vestibulo-spinal tract at Deiter is nucleus in the lower part of the pons and the upper part of the medulla. Through this are connected the nucleus of Bechterew, the dorsal and descending vestibular nuclear and other cerebellar centres.

(ii) The corpora quadrigemina, which are concerned in a higher set of reflexes exercising a controlling influence on those of the first group. Closely linked with them are other optic and oculomotor centres in the lateral geniculate body, the pulvinar of the thalamus, and doubtless the occipital lobes. In birds and fishes, which must maintain equilibrium in relation to three planes instead of two, the corpora quadrigemina are represented by the optic lobes, the most conspicuous part of the mid-brain.<sup>\*</sup>

(iii) The central terminations of nerves of kinaesthetic and tactile sensation. The relative unimportance of the latter is shown by Sherrington's observation that a cat, provided its reflex muscular co-ordination is intact, can walk perfectly even if rendered anaesthetic on the soles of all four feet.

\* But it is a curious paradox that fish are notoriously bad sailors. Specimens sent across the Atlantic for breeding purposes must, if they are to arrive in good condition, be carried in a part of the ship where movement is least. Apparently movements of the body through space which are divorced from the will, and occur unexpectedly, fail to become co-ordinated with other necessary adjustments, such as muscle-tonus. The avian brain, though likewise equipped for voluntary movement in three dimensions, is equally capable of being disturbed by passive movements of a violent or unusual kind. A certain ship's officer had two pet canaries which accompanied him on his travels. 0ne of them frequently spent the first 24 or 36 hours of a voyage drooping listlessly against the bars of its cage, or lying silent and motionless on its side. It was more than once thought to have died; but sooner or later it revived, and exhibited the same cheerful activity as the other bird, which never seemed to be affected in any way.

(iv) Delmas-Marsalet of Bordeaux and Nikitin of Leningrad have recently (Report of International Neurological Congress,
B.M.J., 1935, ii, 270) drawn attention to the rôle of the frontal lobes in equilibration and static innervation.

(4) Fatigue is an inevitable consequence of over-activity.It affects in characteristic ways (a) reflexes, (b) nervecentres, and (c) muscles.

(a) Although the strictly postural reflexes do not readily show fatigue, the maintenance of equilibrium in a moving ship involves other more fatigable reflexes, such as ocular and labyrinthine. But what is called "fatigue" as applied to reflexes is so evanescent that it must be considered to be merely a form of inhibition or "negative induction."

(b) Fatigue of the nerve-centres is quite another matter. The appropriate reflex response gradually loses strength, steadiness, and accuracy. Competitive, possibly antagonistic, reflexes employing the same efferent path may ultimately displace them (Sherrington). Pavlov has shown that fatigue of nerve-cells is closely related to the phenomena of sleep. Apparently exhaustion of a nerve-cell results in some process, condition, or substance, which leads to arrest of its activity -inhibition. Not only so, but the process, condition, or substance, appears to spread to other parts of the nervous system. The importance of sleep in relation to seasickness will be discussed later.

From the above considerations it may be presumed that long-continued repetition of afferent stimuli, whether they be (1) abnormal stimuli, (2) normal but exaggerated or otherwise modified, or (3) a combination or alternation of both, will lead to a more or less generalized inhibition of cerebral centres and a lowered threshold to other afferent stimuli. Inhibition thus induced will affect, among other centres:-

(1) In the cerebral hemispheres, those maintaining attention, interest, and other active mental states.
(2) In the cerebellum, centres of equilibration and muscle-tone.

(3) In the pons and medulla, vestibular, respiratory, and vaso-motor centres, and the manifold connexions of the splanchnic columns and vagal nuclei.

Under the heading of fatigue it is appropriate to consider summation of subliminal stimuli, which, if repeated at short intervals, are capable of producing a positive response (the phenomenon which Exner called "bahnung"). By a process of "immediate induction" (Sherrington) they have the effect of lowering the threshold to allied stimuli. For this reason also, fatigue occurs more quickly after weaker than after stronger stimuli; apparently the threshold of the reaction gradually rises with repetition of stimulation.

(c) Muscular fatigue has been found to follow much more quickly after sudden movements, which require more energy to overcome the tendency of the muscle to resist shortening. It is easy to see how this result will quickly follow the jerky, irregular muscular actions required of one unaccustomed to a ship's movements. Fatigue thus contributes to failure of coordination, in addition, doubtless, to changes in hydrogen-ion concentration and other blood conditions.

#### (c) Effects on the Recumbent Subject.

In those who are lying down there is obviously no great strain on the neuro-muscular apparatus concerned in the maintenance of posture and equilibrium. The effects of movement upon this part of the nervous system are therefore confined to:-

(1) Increased number and unusual diversity of tactile and kinaesthetic stimuli.

(2) Less stimulation of utricles and posterior and superior semicircular canals by the vertical component of the movement, and correspondingly greater stimulation of saccules and so-called

"horizontal" canals. In the dorsal decubitus, with the head tilted at an angle of 30° to the horizontal - a fairly common posture - the "horizontal" (lateral) canals lie in the vertical plane. The familiar fact that seasick patients feel better when lying down is due to the greater sensitiveness of the vertical canals (Maitland, B.M.J., 1931, i, 175).

(3) Little or no tendency to overactivity and consequent fatigue of myotatic and allied reflex arcs, nerve-centres, or muscles. The fact that the onset of seasickness as often as not occurs when the patient is at rest, sitting, lying down, or even asleep,<sup>\*</sup> and consequently not called upon to make any efforts to maintain equilibrium, shows that efforts at balancing play but a small part in the causation. The influence of the labyrinths is considered in more detail later.

#### (d) Effects on both Erect and Recumbent

The results of movement in a storm-tossed ship that arise whether the patient is going about or lying in bed are manifestly the most important, since seasickness may supervene in

<sup>\*</sup> Patients have occasionally told me that they fell asleep apparently well, and, after the sea had become rough, awoke seasick. But it is unusual for seasickness to come on in the dark, provided there are no auditory or other stimuli to indicate the advent of stormy weather. This shows the important influence of ocular stimuli.

either case. These effects are many and diverse. For simplicity they may be grouped under two heads:- (1) Ocular, and (2) Mechanical.

### (1) Ocular Effects.

Perceptions derived from the retinae and the oculo-motor muscles indicate the position and movements of the head in relation to its immediate surroundings. But perceptions from all other receptors (mainly labyrinthine and kinaesthetic, probably also visceral) are simultaneously recording the position and movements of the body in space relative to the direction of gravitational force - movements in which the immediate environment (i.e. the ship itself) participates.

These two sets of sense-perceptions, ocular and other, are incompatible, each competing for the patient's attention; and the greater the movement the greater the conflict. The fact that ocular stimuli are less numerous than their competitors is counterbalanced by their greater precision. Changes of position so minute that they fail to register through other receptors are capable of becoming effectual retinal or oculomotor stimuli.

It might be thought that the conflict of sense-impressions

would be intensified by the accuracy of perception derived from binocular vision. I have tried to eliminate this factor by paralysing accommodation in one eye, but have failed to find any evidence of benefit.

The impact of conflicting groups of sense-perceptions produces effects upon the central nervous system which are complex and far-reaching.

(a) On the Cerebrum. Mental confusion and a sense of bewildered helplessness dominate the field of consciousness. The emotions are disturbed by an instinctive fear of, and revulsion against, the sense of incalculable and irremediable instability. This psychic disturbance is in line with the tenets of the behaviourists (Watson et al.), who hold that the only two sources of inborn fear, as distinct from fear born of experience, are sudden, unexpected noises and loss of support. An unfamiliar, disconcerting commotion is a frequent accompaniment when "the Atlantic's level powers cleave themselves into chasms," while a sense of inadequate support is a distressingly constant feature. Ever since the first Palaeolithic man ventured afloat in a hollow tree-trunk, homo sapiens has been striving to adapt his reflexes to movement in three planes. But his sapient mind travels more easily in four dimensions than his human body does in three. Amid all the luxurious grandeur of a modern liner, the seasick sufferer yearns for the reassuring stability of <u>terra firma</u>. The instinctive intensity of his longing bears witness to the depth of his emotional distress when in anguish he exclaims with Gonzalo that he "would give a thousand furlongs of sea for an acre of barren ground; long heath, brown furze, anything."

Another source of emotional disturbance is traceable to the influence on the emotions of bodily changes arising in response to elaborate - and in this case irreconcilable - groups of reflexes. William James was the first to point out that subjective emotional states come after, not before, concomitant physical changes; it is not that we tremble because we are afraid, but we feel fear because we find ourselves trembling. In other words, the emotion is but the echo of the bodily disturbance. Observations quoted on page 34 show that certain physiological variations commonly occur in consequence of slight movement of the ship before there is any subjective awareness of bodily change.

If the patient, although finding difficulty in keeping his balance, is fit to walk on deck, and is consciously determined to adapt himself to his turbulent surroundings, a certain

measure of harmony can be restored to his confused perceptions if he can be persuaded to concentrate his attention on the horizon while walking, keeping a "blind spot" for the intervening waves. The horizon is the only constant feature amid a welter of bewildering, constantly shifting, forces - the only trustworthy guide to the direction of the pull of gravity. By fixing his gaze upon that, he may find that his legs are now guided by his eyes as well as by his labyrinths. Thus the establishment of a highly complex conditioned reflex is aided by the reinforcement of an unconditioned one.

(b) <u>On Mid-Brain and Bulb</u>. The appropriate response to a given stimulus (in this case a visual image reinforced by kinaesthetic perceptions from the oculo-motor muscles) is the outcome of a well-established conditioned reflex. The action of the reflex involves the temporary inhibition of all other incompatible reflexes. But at the same moment other stimuli, kinaesthetic and labyrinthine, are eliciting equally wellestablished conditioned reflexes whose effectual action involves the excitation of certain nerve-centres which the activity of the first conditioned reflex tends to inhibit. Discordant perceptions, in other words, induce discordant reflex responses. Thus arises conflict between excitation and inhibition. The outcome of this conflict is determined largely by two factors:- (1) the temperament of the individual, and (2) the suddenness or otherwise of the onset of the disturbance.

(1) "Temperament" in this context may be defined as the tendency of the central nervous system to respond to conflicting stimuli in a manner which distinguishes the individual (or. more precisely, one group of individuals) from others. The nature of the response seems to depend upon whether excitation or inhibition is the predominant tendency. The parallel between this condition in the human subject and the reactions of Pavlov's dogs is too seductive to be resisted. It is well illustrated in the oft-quoted case of dogs trained to respond positively to a circle of light thrown on a screen, and negatively to an ellipse. This achievement of discrimination was brought about by the gradual development of appropriate inhibitions. The investigators found that it was possible to cultivate more and more delicate powers of differentiation, up to a certain point. Beyond that, there was a sudden and complete breakdown of the carefully elaborated system of conditioned responses and inhibitions. The further behaviour of the animals was apparently determined by their natural differences in temperament:

(a) The lively, excitable type of dog showed impairment, and even complete loss, of inhibition.

(b) The docile, inactive dog, on the other hand, had its positive conditioned reflexes gradually weakened and finally abolished. Inhibition prevailed throughout all its responses.

There seems little doubt that seasick subjects show a similar tendency to fall into groups according to natural differences in temperament. The restless, emotional type has been compared to the "choleric" and "sanguine" temperaments of Hippocrates. It has equal points of resemblance to the sympathicotonic type of a later epoch. In marked contrast is the vagotonic type, the "phlegmatic" or "melancholic" inhibited, negative, where the other is active, positive. But these are extremes, and the majority of cases fall into countless intermediate groups. The assessment of the relative importance of sympathicotonic and vagotonic elements is more fully discussed later.

(2) As a general rule, my experience has been that when the disturbing stimuli arise suddenly they arouse responses which are predominantly sympathicotonic. Conversely, if the disturbance begins gradually, and is continued for a relatively long period, the responses tend to be vagotonic. This observation also is made with the reservation that most cases are of a mixed type.

### (2) Mechanical Effects.

The purely mechanical effects of passive movement occur both when the body is upright and, to a lesser degree, when it is recumbent. Uniform velocity <u>per se</u> has no disturbing effect: witness the case of aviators, and even their novitiate passengers, who can travel at a steady speed of 200 or more miles per hour, not only without discomfort, but with a very imperfect awareness of movement. The disturbing conditions are acceleration and retardation; and their effects vary in proportion to:

(i) Rapidity of onset.

(ii) Rapidity with which acceleration in one direction
 is succeeded by (a) retardation in the same direction,
 or (b) acceleration or retardation in any other direction.

But movements of this kind do not affect all parts of the body equally. The variable factors are:-

(iii) Mass.

(iv) Mobility.

Movement will thus produce special and distinct effects on such diverse organs and systems as the labyrinths, liver and alimentary canal, brain and spinal cord, cerebro-spinal fluid, and blood. (a) <u>Labyrinths</u>. The labyrinth is the one organ exclusively designed to register, and initiate appropriate responses to, movement. The work of Maitland and others (B.M.J., 1931, i, 171) has abundantly proved that the elaborate reflex mechanism of equilibration activated by vestibular stimuli is not, in the average normal person, adapted to the discrimination of abnormal or excessive stimuli. Overstimulation produces, primarily, nystagmus, with postural and kinetic deviation; and, secondarily, heterophoria, and changes in blood-pressure and pulse-rate, together with the classical symptoms of naupathia, viz. vertigo, headache, and nausea.

Short of pathological changes, there is a certain range of movement or change of position within which the reflexes fulfil their requisite function; beyond that, their responses are merely erroneous. Speaking of "Flying in Fog," G. Youill (quoted in The Listener, Jan. 16, 1935) said: "Many hours of arduous training are necessary before a pilot can accept with confidence the evidence of his instruments and ignore the powerful, but often wrong, messages of his physical sensations."

The occurrence of seasickness without conscious loss of balance, and of difficulty in balancing not accompanied by seasickness, shows that the theory of disturbed balance does not

fully explain all cases. The labyrinths may be subjected to abnormal or excessive movements which produce reflex responses involving certain adjustments not necessarily concerned with the maintenance of balance. For example, sensations referred They to the region of the Eustachian tube have been described. occur most commonly when the ship is pitching badly, i.e., rising and falling. A single, slight, but distinct, click is felt (or heard?) during the phase of descent, which is usually the more rapid of the two. I am able to testify from personal experience that this symptom, when present, occurs invariably on one side, where the tympanum is intact, and never on the other side, where the membrane is destroyed. It may be presumed that a reflex adjustment of intra-tympanic pressure is brought about viâ the otic ganglion and either (1) the tensor veli palatini or (2) the tensor tympani. (If due to contraction of the stapedius, as has been suggested, this symptom would not depend upon the integrity of the tympanic membrane). The afferent stimuli initiating the reflex may originate in the vestibule, the effect being a damping-down of vestibular activity by increased pressure in the tympanic cavity. This would help to explain the benefits claimed in seasickness from firmly plugging each external auditory meatus as far as the tympanic membrane (Lemon, Med. Press & Circ., 1919, Aug. 6, 108).

(b) <u>Liver</u>. Whether the labyrinths or other parts are most affected by movement may depend upon the rate and amplitude of movement, or the rate of starting and slowing, combined with the relative mass and mobility of the various organs. One of the most massive organs in the body is the liver, with an average weight of at least three pounds. Its mobility is proved by alterations in its shape and position which can be produced by distension of the stomach or the adjacent portion of transverse colon. Sudden acceleration and retardation may naturally be expected to combine with the inertia of this mass to produce tension of its supporting structures. Nor is it any more fanciful to suppose that there may also be some molecular disturbance of the liver cells, resulting in disordered function.

G.M., female, act. 24, was seasick for one day, with headache and nausea, but no vomiting. The symptoms entirely disappeared after a single dose of atropin sulphate. Next day the appetite and digestion were normal, but an unmistakable icteric tint appeared in the conjunctivae, lasting for three days.

It is possible that other disorders of liver function may arise similarly. Seasickness has been attributed to "acidosis." by which most writers mean ketosis. But Marrack

(B.M.J., 1931, i, 178) has shown that ketosis is not cause, but effect. It may conceivably follow vomiting (which in a sense is equivalent to starvation) or suspension of normal metabolic activity from other causes. The prophylactic value claimed for antacids suggests that depletion of the alkali reserve may occur apart from ketosis.

(c) <u>Alimentary Tract</u>. The combined effects of mobility and inertia may reasonably be supposed to act also upon the stomach and intestines. For distensibility, and variation in size and position, the stomach ranks first among the viscera, with the possible exception of the gravid uterus. But whereas the uterus is well supported, and grows in thickness as it grows in size, the stomach is pendent, and subject to loss of tone from various causes which lead to stretching and distension.

Some of the most enlightening of recent developments in the conceptions of anatomy are due to x-ray findings, particularly with regard to the mobility of the several parts of the alimentary canal, and the variability of their position. Extreme and unexpected modifications of the cadaveric picture familiarized in the dissecting-room have been found to exist without discoverable sign of disease.

Ryle (B.M.J., 1922, i, 192) found that a stomach radiographed with barium during migrainous nausea was quite inert. Allowing for the weight of barium and its inevitable effect on an atomic stomach, it may be said that this observation leaves it still in doubt whether nausea causes atomy or vice verså. But it is a common experience to find that a patient undergoing an abdominal operation with only local anaesthesia will complain of nausea whenever the slightest traction is exerted on small intestine or mesentery. Recent conceptions of surgical pathology point to the parietal peritoneum as particularly well equipped for the reception and transmission of afferent stimuli.

The phenomena of nausea (and presumably also of its first cousin, anorexia) would therefore seem to be produced in certain cases by mechanical stimulation of the sympathetic nerve-endings. This stimulation will be increased, in a moving ship, by (1) length of mesentery and (2) loaded states of the hollow viscera. The following clinical note is at least suggestive:-

"Miss D.W., act. 27. While sailing to Canada in April 1929 was very seasick. During residence there she had acute appendicitis necessitating operation, followed apparently by peritonitis. Drainage

incisions seem, from the scarring, to have been made in the abdomen anteriorly and in the left flank; these scars are still (October 1930) tender. During the present voyage there has been an unusual amount of rough weather. Cases of sea-sickness under treatment amounted to 10.0 per cent. of all passengers (makes 4.3 per cent., females 19.8 per cent.), but Miss W. has escaped entirely, although the weather has been much worse than when she crossed before. She has had no prophylactic treatment of any kind."

Two possible explanations suggest themselves (excluding the possible influence of other factors quite unknown). Either (1) the appendix had been a focus of toxic absorption which weakened the bodily resistance to noxious stimuli; or (2) the operation had been followed by peritoneal adhesions which subsequently reduced the mobility of the abdominal viscera.

Many seasick patients have appeared to derive great benefit from a tight abdominal binder or many-tailed bandage. It is not always easy to apply this with equal and steady pressure. Failing a binder or bandage, the ventral decubitus sometimes seems to alleviate discomfort referred to the abdomen. So does forcible diaphragmatic breathing, which is merely another means of raising intra-abdominal pressure. The effects of deep breathing may, however, be otherwise explained; disorders of respiratory rhythm are described on page 40. Increased pressure in the splanchnic veins may also have a favourable influence in these circumstances, splanchnic stasis being associated with low blood-pressure, which will be discussed later. Price finds that "the wearing of an abdominal belt is very useful in some cases of hypotension."

As might be expected, the mechanical effects of inertia on the abdominal viscera appear to be more marked in visceroptosis and in patients of the sympathicotonic type, in whom atony may doubtless be presumed to have supervened in consequence of sympathetic stimulation.

(d) <u>Cerebro-spinal Substance</u>. Cerebro-spinal substance, by reason of its consistency, must have a certain amount of mobility. But if seasickness be the accumulated result of a series of minute concussions it is difficult to understand the selective action of the cerebro-spinal trauma, some centres being much disturbed, others escaping entirely. Furthermore, even the slightest degrees of cerebral concussion are followed by some dulling of consciousness, but seasickness is usually accompanied by an unpleasantly augmented sense of awareness.

Nor does recovery from seasickness, whether attributable to adaptation or to cessation of the causative stimuli, manifest any symptoms comparable to the phase of reaction which follows concussion.

According to Hausner and Hoff (Zeitschrift für klinische Medizin, Berlin, 23rd October, 1933, quoted in the Journal of the American Medical Association, 6th Jan. 1934) it is possible that some relationship exists between anxiety states, such as the characteristic dread in angina, and oedema of brain substance.

(e) <u>Cerebro-spinal Fluid</u>. The fluid tissues of the body are doubtless more mobile than solid organs, but their range of movement induced by external forces is limited by the vessels which contain them. Abnormal movements of cerebrospinal fluid may conceivably take place in the direction of the long axis of the medullary canal, the cerebral ventricles, or the subarachnoid and subdural spaces. Headache, vomiting, and vertigo, familiar to most victims of seasickness, are a triad of symptoms commonly following lumbar puncture, and said to be due to hypotension of cerebro-spinal fluid. There is no direct evidence that this occurs in seasickness, except perhaps secondarily to a fall of blood-pressure; but I have found other reasons (discussed under "Headache," page 43) for believing that

some relationship may exist between this symptom and changes in the cerebro-spinal fluid.

(f) <u>Blood</u>. Mass movement of blood, or, what is more probable, the transmission of wave-impulses, from the action of external forces is prevented in the arteries and arterioles by (1) the velocity of the blood-stream arising from cardiac systole, and (2) arterial pressure, which depends mainly upon peripheral resistance maintained by the arterioles. But neither of these factors operates on veins or capillaries, wherein vast accumulations of blood can occur, especially in the splanchnic area during digestion.

If passive movements of the body, combined with inertia and mobility of the blood, are capable of producing any circulatory changes, these will be more readily and more completely effected in the upright position of the body when the vertical component of the movement predominates, because almost all the large veins run in the long axis of the body. (It is a matter of frequent observation that pitching produces much more disastrous results upon the susceptible than rolling).

Furthermore, the changes so produced will tend to be greater where length of body preponderates over breadth; not only because of the axial arrangement of veins, but also because, when the mass of a body is constant, its length increases in

inverse ratio to its width.

In order to investigate the height/weight ratio, 22 adults, ten men and twelve women, were accurately measured. Ten of these (4 men and 6 women) were known to be susceptible to seasickness, while the remaining 12 (8 men and 4 women) were apparently immune. The results are set forth in Table I, from which it will be seen that the average ratio of height in millimetres to weight in kilograms was 30.5 in the susceptible, 25.1 in the immune. Chart I shows still more clearly that the height/weight ratio is higher in the susceptible group than in the immune.

## II. THE FINAL RESULTS OF MOVEMENT.

The fact that a high height/weight ratio prevails among those susceptible to seasickness is open to other interpretations than that of mere mechanical disturbance. The hyposthenic type, distinguished by a high height/weight ratio, is generally recognized to be prone to low blood-pressure. It is not surprising, therefore, to find a fairly constant association of susceptibility to seasickness with hypopiesis. Nineteen cases known to be susceptible, having an average age of 31, were examined either in port, or at sea in calm weather. They were compared, under

identical conditions of posture, fasting, and time of day, with twelve controls known to be immune, whose average age was 30. Each recorded reading is the average of a minimum of five. The results are shown in detail in Table II, from which it will be seen that the mean arterial pressure in the immune group was 123/82; in the susceptible, 114/77.

From what is known of the action of the carotid sinus reflex, it may be inferred that through this or some other reflex agency activation of depressor nerve-fibres (most of which, according to Halliburton, are either bound up in the trunk of the vagus or eventually become connected therewith) may cause vaso-dilatation throughout the distribution of the splanchnic nerves, that being the region most liable to be affected by inhibition of constrictor impulses. Thus, such cardio-vascular changes as may be found are likely to be of reflex origin.

#### (a) Changes in Arterial Pressure.

A recent authority (Keevil, Jnl. R.N. Med. Service, July 1935) said: "In the seasick type the blood-pressure is at all times slightly subnormal, just as the pulse is slow, but during seasickness the blood-pressure has been found if anything to be slightly higher than in harbour." Previous

observers (Biehl, Elder, Fischer, and Flack) have reported a fall in blood-pressure. The results of carefully controlled observations, which I have carried out in various ships, and which form the foundation of this thesis, lead me to the belief that neither of these generalizations is accurate.

For the purpose of investigating this question, ten normal subjects, 5 men and 5 women, were repeatedly examined. in seasickness and in health, ashore and afloat. All were members of ships' crews who were known to be susceptible. in varying degree, to the effects of rough weather. The ages of the men were 15, 21, 31, 43, 44; of the women, 28, 30, 41, 47. 51. Their length of sea-experience ranged from fifteen months to twenty-five years. Thus they all exhibited an extreme degree of susceptibility, or slow adaptability, or both. (I consider it useless to attempt to draw conclusions from the examination of passengers who have not been examined before becoming seasick: even if they are observed after recovery it is impossible to be certain that the arterial pressure, if it has changed. has returned to its usual level).

Every care was taken to exclude the presence of disease which might produce disturbances of blood-pressure. The auscultatory method was used throughout, the apparatus consisting

of a Baumanometer pressure bag (14 cm. wide) connected to a Tycos (aneroid) sphygmomanometer. In calm weather a Baumanometer mercurial instrument was also used as a check on the accuracy of the aneroid. The mercurial gauge is useless in rough weather because of alterations produced in the level of the mercury column by the movements of the ship. As before, each recorded reading is the mean of at least five; this extra precaution is intended to reduce the margin of error to a minimum. and is essential to accuracy because two special difficulties arise at sea: (1) It is far from easy, amid the pandemonium that accompanies really stormy weather, to be certain of the exact points at which systolic and (especially) diastolic pressures occur. (2) Fluctuations in pressure seem to take place, usually associated with the difficulty of securing satisfactory muscular relaxation; these are possibly due to cerebellar reflexes.

The results of these investigations are summarized in Table III, from which it will be seen that six cases showed a fall of arterial pressure, and four a rise. Both systolic and diastolic pressures were affected in all cases. The percentage amounts of rise or fall of systolic and diastolic pressures respectively are analysed in Table IV. Here it is seen that the average change in cases showing a rise of pressure was,

systolic 7 per cent., diastolic 11.2 per cent.; in cases showing a fall of pressure the corresponding figures were 8.6 per cent. and 13.4 per cent. That is to say, diastolic pressures on the whole are more affected than systolic.

The question whether seasickness affects the systolic pressure more, or less, than the diastolic, or both equally, involves a distinction that is of more than casual interest. Lowered systolic pressure with relatively unaltered diastolic would suggest vagal activity (cardiac inhibition), while the opposite condition - a relatively large fall in diastolic pressure - would be indicative of peripheral vaso-dilatation. It may be inferred from Chart II and Tables III and IV that the peripheral factor predominates.

One fact stands out clearly, and that is that arterial pressure does not remain unaltered in seasickness. In some cases it rises; in others it falls. It would appear from a closer study of Tables III and IV that neither rise nor fall is determined by the age of the patient; nor does the extent of change in either direction show any relation to previous deviations from the normal.

These divergences of rise and fall of blood-pressure are best explained on the hypothesis applied to seasickness by Fischer and by Bohec, namely, that disturbances of the

autonomic nervous system are characterized by predominant activity of either the sympathetic or the parasympathetic element. The key to the central problem of seasickness lies in the pithy comment of Bohec (Presse Médicale, 4 Jan. 1930): "C'est qu'il n'y a pas de mal de mer: il y a des maux de mer." It is not the extremes of vagotonia and sympathicotonia that are found, but a host of intermediate types. Since life itself depends upon a perpetual interplay of two opposing forces, the sympathetic and the parasympathetic, it follows that no matter how dominant the one may be, the influence of the other can never be wholly absent. The various "maux de mer" are like the orange tints of the rainbow, which, however yellow, still have a shade of red in them, and yet can never be so red as to lose all their yellow. It is of the greatest importance in the treatment of every case of seasickness to assess as accurately as possible the relative influence of sympathetic and parasympathetic.

To the simultaneous activation of both vagus and sympathetic Bickel has given the name "amphotonia." The cognate problems of differentiation and treatment are complicated not only by this but also by two other factors:-

1. Only a part of the sympathetic or parasympathetic system may be affected.

2. A case may be predominantly sympathicotonic at the outset and become vagotonic later. The reverse may be equally true, but I have not observed fit.

# (b) Pressure-Changes without Symptoms.

During the investigation of blood-pressure changes in seasickness one interesting fact emerged incidentally. Circulatory or vasomotor changes frequently precede the appearance of subjective symptoms. Susceptible cases, examined during rough weather which was not severe enough to make them feel ill, showed blood-pressure changes of smaller degree than were found when they were seasick. That this may be a fairly constant occurrence is suggested by the finding of slight changes during rough weather among those who appeared to enjoy complete immunity. The results are recorded in Table V and Chart III. It is interesting to correlate these observations with the comments on page 14.

#### (c) Capillary Stagnation.

On the assumption that in vagotonia the symptoms of seasickness were due to a fall of blood-pressure, which would eventually show itself in capillary stagnation, I have tried to obtain comparative estimates of venous and capillary blood. In place of red cell counts, haemoglobin estimates had to be used, since the former procedure cannot be accurately carried out in rough weather. On account of the very natural difficulty of securing sympathetic co-operation from seasick victims in this type of investigation, only five readings were made. The somewhat inconclusive results were as follows:-

	С.М.	G.J.	M.T.	E.D.	J.B.
Capillary Hb %	87	80	90	85	94
Venous Hb %	82	80	84	87	90
Difference	5	0	6	-2	4

#### (d) Temperature.

With the further idea that capillary stagnation might have the effect of producing increased differences between oral and axillary temperatures, 29 readings were taken in cases of seasickness, contrasted with readings taken in calm weather, 20 of which were in immune controls and 31 in others known to suffer varying degrees of discomfort in bad weather. The expected results were not found. On the contrary, the mean difference between oral and axillary temperatures in all three groups was only between 0.5 and  $0.6^{\circ}F$ .

A further observation, more relevant to the present line of investigation, was that the susceptible cases occupied a position intermediate between the immune group and the actual sufferers. The importance of maintaining the warmth of the body, not only for the patient's comfort, but as an adjunct to treatment, becomes self-evident. The average temperatures were as follows:-

	Axillary T.	Oral T.	Difference.	
Seasick patients	97.2	97.8	0.6	
Susceptibles	97.6	98 <b>.2</b>	0.6	
Immunes	98.1	98.7	0.6	

### (e) Basal Metabolic Rate.

The foregoing results suggested that a low metabolic rate might be associated with a tendency to seasickness. Using the blood-pressure readings already obtained, estimations of basal metabolic rate were made according to Read's formula, i.e.

B.M.R. = 0.683(P.R. + 0.9 P.P.) - 71.5

In the results plotted on Chart IV, all susceptible cases, whether actually seasick or not, are grouped together in contrast with the immunes. It is evident that, while on the whole the immune cases have a higher basal metabolic rate than the others, the distribution otherwise shows no distinct difference between the two remaining groups. Chart V is a further analysis of the "susceptible" class into vagotonic and sympathicotonic, each group being subdivided according to whether they were to be rated as "seasick" or merely "known to be susceptible." These final results are much more illustrative, and show the following averages:-

Vagotonic, seasick,	5 r	eadings,	av.	B.M.R.	=	-7.2
Vagotonic, susceptible,	6	11	11	11	2	-6.3
Sympathicotonic, susceptible,	9	\$ <b>\$</b>	H	<b>FR</b>	*	-1.4
Sympathicotonic, seasick,	15	11	11	11	=	5.4
Immune,	13	11	H	11	=	6.8

The range among the seasick vagotonics was from -4.3 to -9.8; but the seasick sympathicotonics varied from -9.9 to 21.4. One case in particular showed wide fluctuations in successive readings, viz.: 15.0, -6.5, -6.4, 19.1, -9.9, 15.6, 3.1. Periods of vagotonia apparently alternated with periods of the more predominant sympathicotonia.

The example just quoted illustrates very clearly the importance of early recognition of the dominant element in any case of seasickness, and likewise of its occasional variations. Indications for treatment will be discussed in detail later; it

is enough for the present to state definitely that they are determined by the tendency to vagotonia on the one hand or to sympathicotonia on the other. From the observations already recorded it will be clear that a careful investigation of the state of the blood-pressure yields valuable evidence of the nature of the case. But elaborate investigation is not feasible clinically. for two reasons: (1) Much time is required to eliminate the possibility of hasty and misleading interpretations of the cardio-vascular picture; and the more cases one has to deal with the less time can be devoted to each. Moreover, time is as precious to the seasick patient as to the physician if he entertains any hope of relief. (2) When seasickness has definitely declared itself, few sufferers will willingly submit to the tedious routine of carefully checked blood-pressure readings. Willing co-operation is an indispensable preliminary to the requisite state of mental and bodily relaxation without which blood-pressure readings are valueless.

## (f) Special Symptoms and Signs.

The question then arises: What can be learned from the purely clinical aspect? From a study of several hundred cases I believe that it is possible to form a fairly accurate opinion

of the type to which a case probably belongs; firstly, by attention to detail in the patient's account of the onset of his illness and his description of symptoms; secondly, by the careful assessment of the relative importance of all symptoms and manifest signs to form a composite picture, rather than by the attempt to deal with any one of them symptomatically.

As to clinical history, it must be admitted that it is often difficult to turn the patient's mind back to the earliest dim beginnings of his illness. Premonitory symptoms may have been trivial and transient; they are now swamped and submerged in subconscious memory by a flood of greater suffering which appears to him neither trivial nor transient. The question whether he felt slightly dizzy before his headache began seems to him the height of irrelevance now that nausea has him in its melancholy grip and he is "vexed with a morbid devil in his blood that veils the world with jaundice."

1. <u>Pulse-Rate</u>. The pulse-rate is the easiest and earliest guide to the differentiation of types. If taken with the patient recumbent, and counted for at least two minutes (longer if vomiting has recently occurred), it will often be found to be 50 or less in vagotonics, while in sympathicotonics it is rarely under 80. Estimations of blood-pressure by digital compression

of the pulse are generally recognized to be too illusory to be useful except in extreme cases. Price notes as one of the signs of low blood pressure "an increase of the cardiac rate by more than ten per minute on standing after lying down." This sign was present in 18 out of 28 seasick cases that I examined. But in seasickness all the symptoms are usually aggravated by standing, and relieved by lying down. Irregular spurts of guickened pulse-rate are often found to coincide with wayes of nausea and increased unsteadiness. The only reliable factor is that the percentage increase of pulse-rate on standing after lying down tends to be fairly constant in the same person in health, and may be found to be significantly increased in seasickness. In any circumstances, blood-pressure readings are of value only if they register a definite change. Wilson (B.M.J., 1935, i, 93) records the interesting fact that "one of the most successful of the Everest climbers has a normal blood-pressure of 100/70."

2. <u>Respiratory Changes</u>. These occur very commonly in seasickness, but so far (December 1935) I have not found them to be peculiar to any one type. They are of two kinds:-

1. Transient arrhythmia. Three or four short, shallow respirations are occasionally interposed in the time normally occupied by one. At other times the change is in depth rather

than rate; thus, when the ship is pitching, a particularly big lurch will be immediately followed by a deep, sighing respiration. It is to be noted that these changes are not as a rule accompanied by any variation in pulse-rate.

2. Increase of the pulse-respiration ratio. The normal ratio is usually said to be about 4. One hundred pulserespiration readings selected at random from the records of 17 subjects known to be susceptible, and representing various types when seasick, show the following ranges and average ratios:-

When well: from 2.7 to 4.4; average 3.4.

When seasick: from 2.8 to 6.7; average 4.7.

All readings were taken with the precautions previously mentioned. Fifty control observations in hospital cases free from circulatory or pulmonary disease showed a smaller range, viz.: from 3.6 to 4.7, with an average of 4.1.

3. <u>Vertigo</u>. This is a classical symptom in labyrinthine disease and in rotation experiments. It bulks largely in textbook descriptions of seasickness. Although many sufferers from seasickness complain of "dizziness," it is difficult to get a precise description of the sensations so described. My observations lead me to believe that true vertigo is comparatively rare, and that what many patients suffer from is a confused sense of ocular imbalance, probably due to heterophoria and to the conflict of sense-impressions referred to on page 12. Patients will also describe as "dizziness" symptoms which seem to originate in various forms and degrees of ataxia.

Interrogation of a series of 78 adult patients yielded the following results:-

> Vertigo was severe in 10 cases, moderate in 23 ", slight in 16 ", absent in 29 ".

The average pulse-rates in these four groups were 71, 73, 80, 81, respectively. It would therefore appear that the severer cases of vertigo are vagotonic. In many sympathicotonic patients it is not a primary symptom, but appears to be secondary to nausea and vomiting.

4. <u>Headache</u>. Like vertigo, this is often an early symptom in vagotonics, but in definite sympathicotonia it is more commonly a sequel to nausea and vomiting. Children and young adults rarely complain of it at all. In an analysis of 48 cases in which headache was specifically mentioned by the patient I have found that in 33 (69 per cent.) it was frontal or generalized; these showed an average pulse-rate of 83. In the remaining 15 (31 per cent.) the average pulse-rate was 71, and these complained of headache being occipital (8 cases), vertical (4 cases), or temporal (3 cases). Moreover, 13 of this last group of 15 mentioned vertigo as a troublesome symptom. It therefore appears that the headache associated with vertigo is likely to be of vagotonic origin, and may be occipital, vertical, or temporal, while frontal headache without vertigo is probably sympathicotonic.

It may be appropriate at this point to anticipate a brief comment on treatment. In marked sympathicotonic cases I decided to try the effect of acetylcholine, which is considered to be identical with, or allied to, a vagal hormone, and should therefore, by stimulation of the parasympathetic system, tend to restore the disturbed autonomic balance. The results were encouraging but somewhat variable, with the striking exception of rapid relief of headache. The effect was commented upon by almost every patient so treated, and appeared to be permanent. It proved equally successful in several cases with a vagotonic tendency. Here are two typical examples of bloodpressure readings immediately before, and from 20 to 30 minutes after, the subcutaneous injection of 0.1 gram of acetylcholine:-

N.F., male aet. 32: before, 142/76; after, 132/74. K.C., male aet. 34: before, 114/77; after, 111/77.

The first was a typical sympathicotonic; the second tended towards vagotonia. Each patient volunteered the information that his headache had disappeared almost instantly. This raises the interesting but purely speculative question that headache in seasickness may be associated in some way with changes in the cerebro-spinal fluid. Lemaire and Bioy (Le progrès médical, Nov. 28, 1934, 1871) have found that headache following lumbar puncture is rapidly relieved by acetylcholine subcutaneously.

5. <u>Nausea and Vomiting</u>. Nausea and vomiting, although closely associated in seasickness, are by no means inseparable. Figures collected by Maitland (B.M.J., 1931, i, 172) covering 108 cases, show the following relative frequency:-

Vomiting with nausea52,Vomiting without nausea34,Nausea without vomiting22.

According to these figures nausea, either alone or combined, occurs in about 69 per cent. of all cases of seasickness. Since, when both symptoms are present, nausea almost always comes first, it may be said that about 70 per

cent. of cases of nausea are followed by vomiting, and 30 per cent. are not. The degree of relief following vomiting is an important variant in seasickness.

In the vomiting of the ordinary acute gastric disturbance, relief of nausea usually occurs when the stomach has been completely emptied, but not before. In the vomiting of seasickness the stomach may be empty from the beginning, and all that results from vomiting is a small quantity of secretion, usually mucous in character, perhaps tinged with bile. Yet each act of vomiting, however frequently it recurs, is usually followed by a brief respite from nausea.

Relief afforded by the mere act of vomiting is reasonably explained on the assumption that nausea is associated with a condition of gastric atony (see page 22) which is temporarily abolished by, <u>inter alia</u>, contraction of the muscular layer and/or relaxation of the cardiac orifice. When the muscular fibres relax again, nausea returns, and vomiting is repeated. Sometimes the efforts to accomplish the act of vomiting result in aerophagy, and attempts to eructate, if successful, give a certain amount of relief. Clinically the condition is very similar to the functional gastric disorder met with in emotional states. I have often found that seasick patients who complained of nausea and frequently-repeated vomiting were of the sympathicotonic type.

The vagotonic patient, on the other hand, often gives a history of vomiting on one occasion only, or at long intervals. The act tends to be sudden and violent, unheralded by nausea or other aggravation of the general feeling of malaise. Presumably the gastric musculature is active and irritable, while the sphincters are readily relaxed. The condition is comparable to the expulsive act of "cerebral" vomiting, which is characteristically unaccompanied by nausea. Unmistakable benefit often results in these cases from eating very small amounts of food, especially taken dry, and very thoroughly masticated. The determining factor is probably a diversion of gastric activity in less mischievous directions.

I have at various times, using test papers containing methyl orange, tested vomited matter for the presence or absence of free hydrochloric acid; but the secretion of acid seems to be subject to too many variable factors to be of any help in distinguishing one type of seasickness from another.

It is usually taken for granted that the seasick person will not want to smoke. To the sympathicotonic patient the very thought of tobacco is nauseating. Yet in stormy weather I have seen sufferers from headache, vague "dizziness," and malaise with loss of appetite, who could still find solace in a cignrette. These were doubtless extreme vagotonics, and less

liable to be disturbed by the effects of smoking. Izod Bennet has said that "there is little doubt but that tobacco, and particularly cigarettes, tend to produce pylorospasm." It is probably through no chance coincidence that all my typically vagotonic cases were heavy smokers.

In the attempt to reach an explanation of these phenomena, I have studied the effects of vomiting upon nausea in one hundred consecutive cases of seasickness with vomiting seen on various ships and under varying conditions.

Percentages are proverbially fallacious, but at least these figures are definite enough to suggest that vomiting followed by relief points to vagotonia, whereas repeated vomiting with continued nausea is typical of sympathicotonia. It is not without significance that 11 out of the above-mentioned 37 vomited once only, whereas those who were most doubtful of the relief afforded by vomiting were usually those who had vomited most frequently. 6. <u>Sommolence</u>. Sleep, according to Hess, is a condition of sustained parasympathetic tone. But in the treatment of sympathicotonic cases of seasickness I have repeatedly used acetylcholine, which is a specific parasympathetic stimulant, without observing any signs of a hypnotic effect. Sleep, however, has an important bearing on the problems of seasickness. This is shown in two very frequent observations:-

(i) Sleep often has a remarkably recuperative virtue, apparently favouring in some way the restoration of normal autonomic balance. There is no reason to believe that any of the stimuli which bombard the nerve-centres of the recumbent subject are removed, or to any extent prevented, by sleep. But the generalized inhibition which accompanies sleep seems to have the effect of damping down the reflex responses or of diverting them along other paths. Furthermore, the effect is not limited to the period of sleep, but often continues for some time afterwards.

(ii) Drowsiness and lethargy are very marked in some cases; others exhibit mental hebetude without actual somnolence. Of 84 adults guestioned on this subject, 50 (59 per cent.) reported no unusual drowsiness; 14 (17 per cent.) complained of broken, restless sleep, in some disturbed by dreams; the remaining 20 (24 per cent.) felt unusually sleepy, although

no drugs of any kind had been taken. It is noteworthy that the lethargic group showed an average pulse-rate of 69; among the restless the average was 80; the average of the total number was 78. This seems to point to some definite relationship between somnolence and vagotonia.

#### III. THE ESTABLISHMENT OF IMMUNITY.

It is customary to discuss the actiology and treatment of seasickness on the assumption that it is a pathological condition. Gihon (U.S. Navy) estimated that about 5 per cent. of people are immune. In other words, given the conditions favourable to the development of seasickness, approximately 95 per cent. will suffer. A disorder which under appropriate conditions afflicts such a large majority would therefore be more precisely described as a normal response to an abnormal environment. Furthermore, relief of the distress usually tends to occur spontaneously; this likewise is part of the normal response.

The establishment of immunity is Nature's cure; and the whole aim of treatment should be to expedite this process. A passenger sailing from Dover to Calais may be shielded from discomfort by being drugged until he is unaware of the very existence of the ship; but it will not be disputed that on an Atlantic voyage something more radical is desirable.

In venturing to think that we may be able to expedite Nature's methods we are admittedly treading on difficult ground. It is necessary first to have some clear idea of how the process of adaptation comes about. If the conception of seasickness as a normal response to an abnormal environment be admitted, the process of adaptation through which one acquires one's "sea-legs" involves the establishment of a group of what Pavlov ("Lectures on Conditioned Reflexes") calls conditioned responses. Since it is impossible to explain the phenomena of seasickness by any other hypothesis than that of a series of reflex responses, and since the forces acting on the susceptible novice and the seasoned sailor are the same, it follows that adaptation depends upon changes in one or more of the following :-

<sup>\*</sup> The distinction is made with this reservation (such are the vagaries of seasickness), that these two may occasionally change places.

1. Receptors,

2. Afferent paths,

3. Sensory centres,

4. Connexions between sensory and motor centres,

5. Motor centres,

6. Efferent paths,

7. Effector organs,

8. External conditions influencing reflex activity.

If the effects produced upon the receptors of the seasoned sailor by external stimuli are different from those occurring in the novice, it may be safely assumed that the difference is quantitative only. That is to say, it is in the direction of either (a) greater or (b) less intensity.

(a) If the effects of stimulation become more intense, it might appear that immunity to seasickness consists in an acquired sensitivity to stimuli formerly subliminal. This would indicate a lowering of the threshold of the receptors. But if this were so, fatigue of the reflexes would occur more readily than in the normal; which is not in conformity with observed facts.

(b) If, on the other hand, the effects of stimulation of the receptors become less intense, it follows that adequate

reflex response can be maintained only by a corresponding increase in the activity of the efferent part of the reflex arcs involving the countless adjustments necessary for coordinated movement. In this event one must postulate a lowering of the threshold of the afferent centre for effectual stimuli; an assumption which is likewise untenable on the grounds of fatigue of the reflexes.

It therefore follows that adaptation does not involve changes in the receptors. Parallel reasoning applies to the afferent paths, the efferent paths, and the effector organs; also to the possibility of increased or diminished receptivity of the sensory centres.

The possibility of a change of direction of afferent impulses within the brain itself claims consideration. For the purposes of this argument let "affectual movement" describe that degree or character of movement which is capable of producing the minimum degree of seasickness in the normal, <u>unhabituated individual</u>. It will be granted that such affectual movement causes certain temporary physiological changes, and a certain state of activity, in the cells of some part of the brain.

While this is taking place, the brain is receiving (either at the same centres or wholly or partly in other

centres) stimuli which in the absence of affectual movement would reflexly result in (to take one example) the maintenance of equilibrium. According to Pavlov's theory of the establishment of conditioned reflexes, the dominance of cerebral activity produced in the nerve-centres activated by affectual movement causes the less obtrusive stimuli (i.e. those normally resulting in reflex equilibration) eventually to be conducted to these same centres. Each successive application of the combined groups of stimuli contributes to the approximation of their centres of reception in the brain. either (a) directly, by a change in the direction of the afferent path, or (b) more probably indirectly, by the establishment of synaptic connexions between (1) the afferent fibres of the reflex arcs normally concerned in equilibration and (2) the cells activated by the affectual movement.

In this or some such way new nerve-cell connexions are gradually established in the cerebrum for the reception of stimuli normally productive of reflex equilibration. But there is no reason to suppose that the reflex activity of the mechanism maintaining equilibrium does not continue. It follows that with each step in the establishment of afferent tracts leading to the centre of dominant activity equivalent changes take place in the efferent paths, until finally the

reflex maintaining equilibrium has its cerebral centre transferred to the cells activated by affectual movement. In consequence of this change, impulses transmitted to the cerebral cells by affectual movement now produce excitation of the efferent nerve-fibres of the reflex arc which governs equilibration. The reflex response is exactly the same as when these centres are stimulated normally.

The establishment of new paths will follow the same course whether the affectual stimuli originate in the labyrinths or elsewhere.

Finally, there remain to be considered the conditions outwith the reflex arc which influence its activity. Maitland (B.M.J., 1931, i, 175) quotes Malan's observation, in rotation experiments, that after frequent repetition of abnormal vestibular stimuli nystagmus and other responses failed to appear; and explains this as due to "cerebral control, an increasing ability to inhibit the effects of the abnormal excitation of the vestibule." Malan's explanation was fatigue, but fatigue of reflexes is a short-lived phenomenon, whereas adaptation tends to increase, and may persist indefinitely. Head says of the process of adaptation that "the stimuli from the peripheral end-organs no longer dominate the field of response. They are controlled and suppressed, not by the will.

but by that power of adaptation which is one of the most potent factors in the activity of the nervous system." The importance of this fact is that whether the afferent stimuli initiating the reflex responses of seasickness be vestibular, cerebral, cerebellar, cardiac, vasomotor, or visceral, or due to chemical changes in the blood or to the interaction of various endocrine glands, the process of adaptation is essentially the same.

The details vary somewhat according to the potency of the conditioned stimulus supplied by the movement of the ship. This stimulus either is, or is not, slight enough at the beginning of the process to rank as one to which the nervous system is physiologically indifferent.

The strength of stimulus to which the nervous system is indifferent obviously depends upon the inborn character of the individual nervous system, and the resultant effect of external conditions, some of which may be favourable and others unfavourable. It is also relative to the strength of the stimuli that have preceded it. A slow, imperceptible increase of strength of stimulus is the ideal road to adaptation, but seldom encountered. On the other hand, I have witnessed a gale at sea when the wind winnowed the susceptible like autumn leaves; on the next day the sea was comparatively calm, and

many ventured forth fully recovered, unaware that, but for yesterday's storm, to-day's swell would assuredly have laid them low.

If the stimulus of the ship's movement is an "indifferent' one, the process of adaptation consists in the development of a conditioned reflex whose responses are positive. If the stimulus is not "indifferent," a conditioned reflex must be established whose responses are negative. In the first case extraneous stimuli interfering with the development of the reflex are inhibitory; in the second case extraneous stimuli interfere with the development of inhibition (which is the essence of the "negative" reflex), and are therefore called disinhibitory. In other respects each follows closely the course of the establishment of conditioned reflexes, and is subject to the same four fundamental requirements, namely:-

(1) The simultaneous action of the conditioned 'stimulus and the unconditioned stimulus already established as the activator of the desired reflex. This is summed up in the commonsense axiom that one cannot expect to get one's sea-legs by lying in bed. It provides one reason why seasickness is less common among the crew of a ship than among passengers. Walking "with" the feet, not merely "on" them, increases the range and intensity of proprioceptive stimuli.

thus aiding the reinforcement of the conditioned stimulus.

(2) The exclusion of all extraneous stimuli capable of producing particular responses antagonistic to the action of the conditioned reflex which it is desired to establish. This includes an infinite variety of disturbing stimuli, ranging from the thundering of a stormy sea, or the creak of straining beams, to the malodorous emanations from galley ventilators, or toxins absorbed from a diseased gall-bladder. Rough weather at sea usually means closed portholes, and consequently, even in the best-ventilated ships, a certain interference with air-exchange. It is possible that low barometric pressure may also affect the unusually sensitive. The disturbing effect is all the greater if the extraneous stimulus finds a ready outlet: the predisposition of the "bilious" stomach is a familiar example. Another reason for the relative immunity of crew as compared with passengers is that continued occupation sets up a barrier against extraneous stimuli.

Not only will intrusive external stimuli readily hinder the development of a conditioned reflex (especially one so complex as that of adaptation), but they may disrupt one that has been previously established. Even the most hardened sailor may fall a victim to seasickness if his health is impaired. Such disturbances resulting from extraneous stimuli are due solely to interference with inhibition. The outcome is seasickness. But it is noteworthy that unusually strong stimuli strike deeper, and inhibit, not the inhibition, but the reflex itself. I have had personal experience of a storm at sea where at the first suspicion of real danger all the despondency of seasickness was completely obliterated in an ecstasy of hymn-singing.

(3) An optimum range of intensity of the conditioned stimulus. If the movements of the ship never exceed a certain minimum, no conditioned reflex can be established. Conversely, if they exceed a certain maximum, the establishment of appropriate conditioned responses becomes increasingly difficult. In this connexion it should be remembered that different parts of a ship at sea are subjected simultaneously to movements differing considerably in character and extent.

(4) A receptive state of the nervous system. Among the factors militating against this are pathological conditions which also come into the category of disturbing extraneous stimuli mentioned in (2) above. Detoxication is an important preliminary to any form of treatment designed to encourage adaptation. A loaded colon, or sugar or acetone in the urine will, if overlooked, frustrate all efforts to establish tolerance. Furthermore, the routine use of hypnotics, whether for prophylaxis or for treatment, defeats its own object when that is the acquisition of permanent immunity rather than the temporary protection of the patient from the effects of an uncongenial environment. Certain qualifications of this statement will be explained later.

When the stimulus of the ship's movement is from the outset, or quickly becomes, one to which the nervous system is not indifferent, i.e. one which tends to produce its own particular series of unconditioned responses, the adjustments involved in the process of adaptation are largely of a negative character, inhibitory.

It is here that wise therapy seeks to follow Nature. Responses involving inhibition reveal the innate differences of the individual nervous system, distinguishing the "melancholic" from the "choleric," the vagotonic from the sympathicotonic. If we bear in mind that there is none so melancholic that he has nothing of the choleric in him, and no vagotonic without some vestige of a sympathetic nervous system, we can learn much from these extreme types of the fundamental principles of treatment.

(A) The placid temperament (vagotonic) yields more readily than the excitable (sympathicotonic) to the development of inhibitions. Indeed, my observations of extreme cases lead me to believe that the tendency to inhibition is often excessive: witness the lethargy and depressed basal metabolism already described. Excessive inhibition may be attacked from one or both of two directions, (i) depressing the inhibitory forces, (ii) stimulating the processes of excitation.

(i) The depressant action of the alkaloids of belladonna on the parasympathetic system is well known. There is still some controversy as to whether atropin or hyoscin is the more efficacious, or whether they are not in fact fundamentally identical. My own experience is that the tincture of belladonna is better than either of the alkaloids. which are best reserved for cases where the stomach rejects fluids of every kind. Keevil (Jnl. R.N. Med. Serv., July 1935, 228) records that "20 minims of the tincture may be given three times a day without toxic effect and with relief of seasickness." I have usually found that if no obvious relief follows a dose of 30 minims spread over four hours the patient will respond better to other treatment. When vomiting is very readily provoked, a useful method of inhibiting the vagus is to place under the tongue, by means of a pipette, 3 or 4 drops

(not minims) of a 1.0 per cent. solution of atropin sulphate, which is equivalent to the now unofficial Liquor Atropinae Sulphatis. It is rapidly absorbed, does nothing to excite vomiting, and is quicker and more convenient than hypodermic injection. Suppositories containing hyoscin (e.g. Vasano) are also valuable.

(ii) In the early stages of vagotonic seasickness there is undoubted value in stimulants, such as strychnin, or caffein either medicinally or in the form of strong tea or coffee. The effect of adrenalin is too transitory to be of much help. I have not yet been persuaded of the efficacy of ephedrin. Vigorous exercise, preferably in the fresh air and in the form of some deck-game which offers distraction as well, has, I am convinced, saved the self-respect of many a wavering vagotonic.

It is in these cases that the routine use of cerebral depressants is to be deprecated. The patient needs every encouragement to strenuous exertion in order to overcome his inhibitory tendencies. It has already been pointed out that vagotonics, even when frankly seasick, derive great benefit from eating a little - greater benefit than is to be explained by the nutritive value of what they eat. Therefore nothing should be given which impairs appetite or digestion. (Inci-

dentally, there are few greater offenders in this respect than the ever-popular chloretone). Finally, if there is any drug which the vagotonic, usually lethargic to the point of somnolence, does not need, and should not have, it is a hypnotic. His widespread inhibitions manifestly call for correction, not encouragement.

It is variously estimated that vagotonia is more common in seasickness than sympathicotonia. In my experience it is certainly more common among men, especially those who have been long at sea without acquiring much immunity. But sympathicotonia is more common in women and children. (Although infants, having not yet grown to orientation, are immune, I have not found the absolute immunity in other children that is generally attributed to them. If the movement begins early in the voyage, they are as susceptible as the average adult; but given a favourable environment they become adapted with astonishing rapidity).

The idea of the prevalence of vagotonia may be due to the fact that long before the description of vagosympathetic states by Eppinger and Hess in 1910 belladonna and its alkaloids were used empirically in the treatment of seasickness. There was no suspicion then that the sympathetic system also played

its part. Another reason may be that the action of belladonna and its alkaloids is not confined to depression of the parasympathetic system; large doses favour the complete abolition of gastro-intestinal activity.

Pace (Minerva Medica, 22nd Sept. 1929), using the total alkaloids of belladonna in 28 cases of persistent vomiting and 77 cases less grave, claimed successful results in all. He treated 79 cases prophylactically, reporting only two failures. This makes 182 successes out of 184, or 98.9 per cent. But seasickness is no more amenable to "penny-in-the-slot" treatment than any other malady. I have treated cases where atropin has without doubt arrested vomiting, but with his mouth and tongue parched, his throat too dry to swallow, and his field of vision a confused blur, the last state of that hapless patient was worse than the first. These cases are not true vagotonics.

(B) The treatment of the excitable (sympathicotonic) subject is in essence the converse of that of the vagotonic. Inhibitory responses have to be developed and encouraged in every way possible. Inadequacy of inhibition may be dealt with (i) by depression of sympathetic activity, (ii) by stimulation of the parasympathetic, or (iii) by a judicious

combination of both methods.

(i) It is in this sphere that sedative drugs are of the greatest value. If the patient's type can be surmised before sailing, sedatives are doubly useful as a form of premedication to prepare him or her for the ordeal of the voyage, which is commonly approached with all the uneasy qualms of the patient prepared for the operating-table.

Chloretone, in the proprietory "Mothersill," ranks high in popularity. It has recently (Gartner, Therapie der Gegenwart, Aug. 1934) been vaunted as a specific sedative for the vomiting centre. The barbiturates are usually well borne, but some of them have an unsavoury reputation for toxicity. In seasick, but otherwise apparently healthy, sympathicotonic patients I have used veronal, phenobarbital, gardenal, sodium emytal, somnosal, and nembutal, with fairly satisfactory results. The last is, in my experience, one of the best. It is true that sometimes there is a period of restlessness following the hypnosis, but this has always been slight; nor does it necessarily mean a return of the symptoms.

McLaughlin (Can. Med. Assoc. Jnl., May 1935,xxxii, 544) reports favourably on the value of nembutal in 70 cases. He classified them according to whether the dominant symptom was

(1) headache (15 cases) or (2) vomiting (55 cases). The second group gave the better results; 88 per cent. are stated to have improved. One suspects that the first group, with headache more prominent than vomiting, were vagotonic and not suitable cases for this treatment.

One serious disadvantage, in my experience, applies to most hypnotics used in the treatment of sympathicotonic seasickness: the benefits to the patient last only as long as the action of the drug. Natural sleep, on the other hand, often has a distinctly restorative effect.

This objection applies scarcely at all to bromides, which I have found to be the most reliable of all sedatives. It is interesting to recall that Pavlov found bromides to have a specific selective action upon the cerebral cells involved in his experimental dogs. When inhibition had been experimentally impaired (cf. page 16), rectal administration of bromide not only led to its restoration, but caused the sonditioned responses to be even stronger than before. In seasickness, I have often found triple bromides exceedingly satisfactory, prescribed in half-hourly doses of at least  $7\frac{1}{2}$ grains. Emphasis on the importance of the patient's taking the medicine with the utmost regularity helps to distract his

attention from distressing subjective symptoms. It is possible also that the frequent and regular (i.e. monotonous) repetition of this "stimulus" favours the development of inhibitory influences. The effervescent tabloid "Tri-bromid" is an agreeable alternative.

Even in the most obstinate cases, bromides seldom fail if combined with chloral hydrate. I have found that in the highly excitable patient bromides and chloral are absorbed even more quickly and surely by the rectum than by the mouth. The beneficial synergistic action of these drugs is possibly explained by the fact that bromides have been found to be without effect on the decerebrate animal, while chloral hydrate acts as well as in the normal animal, or even better. Apparently bromides act on the cortex, chloral on the thalamus and/or brain-stem; one will therefore favour inhibition by obstructing distracting stimuli while the other slows down reflex activity.

It seems hardly worth mentioning that all efforts at sedation must be reinforced by the careful exclusion of all disturbing (positive) stimuli which tend to interfere with the (negative) process of inhibition. But it is just in this respect that many efforts lead to failure and disappointment. Auxiliary measures include protection, for a time at least, from every visual, auditory, or other stimulus that it is possible to exclude.

Even when all efforts to check vomiting are fruitless, I have found that sedative treatment brings a certain degree of amnesia, so that the patient, after recovery, can contemplate the return voyage with fewer misgivings.

(ii) Stimulation of the parasympathetic system is often a more satisfactory method of overcoming sympathicotonia. Even the most excitable patient will in time become exhausted by repeated vomiting. It then becomes desirable to have some other weapon in our armoury than varying degrees of narcosis.

In nine definitely sympathicotonic cases I found that the average fasting blood-sugar was 0.12 per cent. This suggested that the anabolic activity of the pancreas, which is closely linked to the parasympathetic system, might be deficient. Accordingly I tried small doses of insulin (5 to 10 units) as a means of parasympathetic stimulation. The results appeared to be beneficial, but it is difficult to assess their real value. The hypodermic syringe is a potent vehicle of suggestion. There is no doubt that pilocarpin is often effective in doses of 1/8th to 1/6th of a grain hypodermically, provided none of the usual contra-indications is present. It is much more useful if given early. Combined with bromides, and given in half-hourly doses amounting to as much as a quarter of a grain in four hours, I have found it is not only well tolerated but wholly beneficial, with no unpleasant after-effects.

In the same manner I have used ergotinin, at other times physostigmin, and recently its isomer prostigmin, in cases where the blood-pressure seemed low; but I have not found any of them superior to pilocarpin, or so well tolerated by the stomach. The Sandoz preparation of ergotamin tartrate ("Femergin") has benefited more than one case in my hands, in doses of 1 mg. (0.5 c.c.) intramuscularly. The benefits of preparations of ergot, which are believed to paralyse the motor terminations of sympathetic nerves, suggest that a high degree of sympathetic activity prevails in many cases of seasickness; and may also explain the extreme rarity with which abortion occurs in seasickness in spite of the profound metabolic disturbance that often ensues. It also suggests that sympathicotonia is commoner in women than vagotonia; which confirms the experience already mentioned.

The most rational, and in my experience the most effective, method of parasympathetic stimulation is by acetylcholin. As a specific vagal hormone it stands in the same relation to the parasympathetic system as adrenalin does to the sympathetic. Its action on blood-pressure is that of a vaso-dilator. Fulse and blood-pressure readings before and after subcutaneous administration of 0.1 gram of acetylcholin are shown in Table VI. The pulse-rate was reduced in all cases. One systolic and two diastolic readings were unchanged; in all other cases blood-pressure fell.

The beneficial action of acetylcholin on headache has already been described (page 43). In addition, patients have told me that it abolished their sensations of abdominal discomfort, symptoms which were very constantly present, even in the absence of definite nausea. I have also been told that it helps in large measure to restore that feeling of well-being which is noticed only by its absence, and the loss of which is the first hint the patient gets that all is not well with him.

One typical sympathicotonic, a man of unusual sensitiveness and perception but no medical knowledge, mentioned without hesitation "a numb feeling at the back of the tongue"

within five minutes after 0.1 gram of acetylcholin, and described with enthusiasm the miraculous and instantaneous disappearance of "a cold in the throat" which had added to the misery of his seasickness. The latter observation probably relates to some dulling of pharyngeal sensation which was restored by activation of the pharyngeal plexus. The involvement of the posterior part of the tongue suggests that the glossopharyngeal nerve, which arises from a centre in the medulla contiguous to that of the vagus, may also be involved in autonomic imbalance.

(iii) It has been repeatedly pointed out that most cases of seasickness are amphotonic, combining both vagotonic and sympathicotonic elements. It therefore follows that the best hope of success in treatment lies in a judicious combination of remedies suited to both extremes, particular attention being paid to that which predominates at the time. It must also be remembered that prolonged seasickness sometimes presents a kaleidoscopic picture which changes from day to day; and previous knowledge of a patient, even in seasickness, is not always a sure guide to the nature of his future responses. He may be taken unawares by his first attack, presenting a typically vagotonic picture; next time, under apparently identical external conditions, excitement and apprehension so act

upon his nervous system as to determine an equally characteristic sympathicotonic response.

An important advance in the right direction is marked by the introduction of "Bellergal" (Sandoz). This preparation contains belladonna alkaloids combined with ergotamin and luminal. The principle of combining belladonna with ergotamin is sound, but the addition of luminal is questionable for two **reasons:** (1) Of most seasick vagotonics it can be said that if a small dose of luminal does them no harm it certainly does them no good. (2) Individual tolerance, in my experience, varies more with luminal than with either belladonna or ergotamin. Luminal is a popular form of self-medication among many Atlantic travellers, and I have encountered various degrees of addiction. Many of these could have got no cerebral sedative effect from Bellergal until they were on the verge of alkaloidal poisoning. An even greater objection arises in the case of the patient not habituated to luminal, if his symptoms and signs show pronounced vagotonia or sympathicotonia. Bellergal contains bellafoline 0.1 mg. and ergotamin twetrate 0.3 mg. to 20 mg. of luminal. Now, there are many vagotonics who require in one day as much belladonna alkaloid as is "balanced" (sic) in Bellergal by 3 or 4 grains of luminal. Similarly, the sympathicotonic who takes enough ergotamin to

give him a chance of relief is in equal danger of becoming completely narcotized.

The second objection applies also to the simultaneous administration of belladonna and ergot; and applies, indeed, to any stock remedy combining two or more drugs with different (though not strictly antagonistic) actions. It must be remembered, when we speak of vagotonia and sympathicotonia, that fundamentally these are, in their extremes, pharmacological concepts rather than clinical entities, having been based originally on the effects of artificial stimulation or depression by drugs with a selective action, such as adrenalin (sympathetic excitant), atropin (parasympathetic depressant), physostigmin, pilocarpin, and ergotamin (sympathetic depressants). The term sympathicotonia implies undue sensitiveness to adrenalin. or to any other substance, condition, or circumstance having a stimulating effect upon the sympathetic system. This clearly includes belladonna and its alkaloids, which weaken the compensating effect of the parasympathetic. Therefore in seasickness the sympathicotonic requires very much less belladonna and more ergotamin, just as the vagotonic requires less ergotamin and more balladonna, than can ever be contained in any combination devised for use in all cases.

This searching criticism of one of the most useful single preparations available for the present-day treatment of seasickness is merely intended to emphasize the exceedingly important point that ideal treatment can seldom be carried out by any single preparation. The sole exception is the rare case which shows neither symptoms nor signs that can be classified as either vagotonic or sympathicotonic.

It is a favourite gibe that the multiplicity of remedies proves the futility of them all. But this is not necessarily true of seasickness, for the very evident reason that there is no single, invariable cause, but a large and very variable number of causes. It is only chance (by which we mean a combination of circumstances which we can neither foresee nor fully understand) that determines which of these causes will play the leading rôle. Therefore a panacea against seasickness is nothing but an idle dream.

The oft-quoted aphorism that we are treating, not diseases, but patients, is as apt in this context as in any other. Bearing in mind the dual nature of man (dual, that is, from the point of view of the physiologist) we can hardly fail to recognize it when wind and waves conspire to lay bare his innermost physiological responses. The wise physician sets

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out to treat seasickness with a pocketful of diverse remedies which he will combine according to his judgment, after a careful study of the clinical picture presented by the patient. By the very complexity of the forces that confront him he knows better than to expect immediate success from his first attack upon them. But he has two barrels to his gun, for experience has taught him that he may have over-estimated the importance of one aspect of the disorder, or completely overlooked another. It may be that the vagotonic signs which at first declared themselves so unmistakably have obscured some far-reaching disturbance of the sympathetic system. Centuries of patient progress separate the double-barrelled gun from the blunderbuss.

## Table I

21-5 5 1915 20

75.

### Ratio: <u>Height in millimetres</u> Weight in kilograms

Susceptible	Immine			
D.H. male 30.9 F.M. " 31.9 A.B. " 26.4 J.P. " 26.8 B.T. female 31.9 S.W. " 35.4 E.H. " 30.6 S.C. " 29.9 E.J. " 32.8 E.G. " 28.0 • Average: 30.5	H.S. male 21.9 J.C. " 25.1 F.H. " 25.5 J.L. " 28.4 C.J. " 28.0 A.M. " 20.2 F.P. " 29.0 J.S. " 21.1 M.S. female 25.1 M.Q. " 26.5 M.G. " 26.2 M.P. " 24.4 Average: 25.1			

#### Table II

#### Mean Arterial Pressures, in port, or at sea in calm weather.

and the second second		Age	Systolic	Diastolic
Immune Men	H.S.	24	122	68
	J.C.	26	124	78
	F.H.	27	124	82
	J.L.	20	122	83
	C.J.	39	134	80
	A.M.	19	120	94
	F.P.	42	138	83
	J.S.		126	90
	Avera		126	82
Immune Women:	M.S.	32	118	82
Linductie women.	M.Q.	35	124	88
	M.G.	26	112	74
	M.P.	37	118	81
	Avera		118	81
Susceptible Men:	F.M.	31	124	90
Subceptitore ment	A.B.	21	123	81
	J.P.	43	112	78
	F.H.	17	115	76
	R.C.	25	106	74
	C.L.	24	126	96
	D.H.	15	109	73
	F.G.	37	121	88
	N.L.	44	130	92
	K.C.	34	112	75
	Avera		118	82
Susceptible Women:	B.T.	41	103	62
Subceptible	S.W.	30	104	60
	E.H.	23	116	74
	S.C.	28	120	70
	M.S.	28	110	72
	E.J.	30	103	70
	M.O.	47	106	74
	M.R.	41	107	. 79
	E.G.	51	117	72
	Avera		110	70

# Table III

Arterial Pressure Changes in Seasickness.

	Well	Seasick
Men: D.H. aet. 15 A.B. " 21 F.M. " 31 J.P. " 43 N.L. " 44	110/72 128/92 123/91 112/78 129/91	121/79 114/74 109/71 109/73 144/102
Women: M.S. " 28 E.J. " 30 B.T. " 41 M.O. " 47 E.G. " 51	110/71 103/65 103/62 116/77 123/82	112/82 108/70 91/56 104/69 116/72

#### Table IV

#### Percentage Rise or Fall in Arterial Pressure during Seasickness.

		Systolic	Diastolic		
% Rise:	D.H.	10.0	9.7		
	N.L.	11.6	12.1		
	M.S.	1.8	15.5		
	E.J.	4.8	7.7		
	Average:	7.0	11.2		
% Fall:	A.B.	10.9	19.6		
	F.M.	10.4	22.0		
	J.P.	2.7	6.4		
	B.T.	11.6	9.7		
	M.O.	10.3	10.4		
	E.G.	5.7	12.2		
	Average:	8.6	13.4		

#### Table V

Arterial Pressure Changes in Rough Weather Before and After Onset of Seasickness.

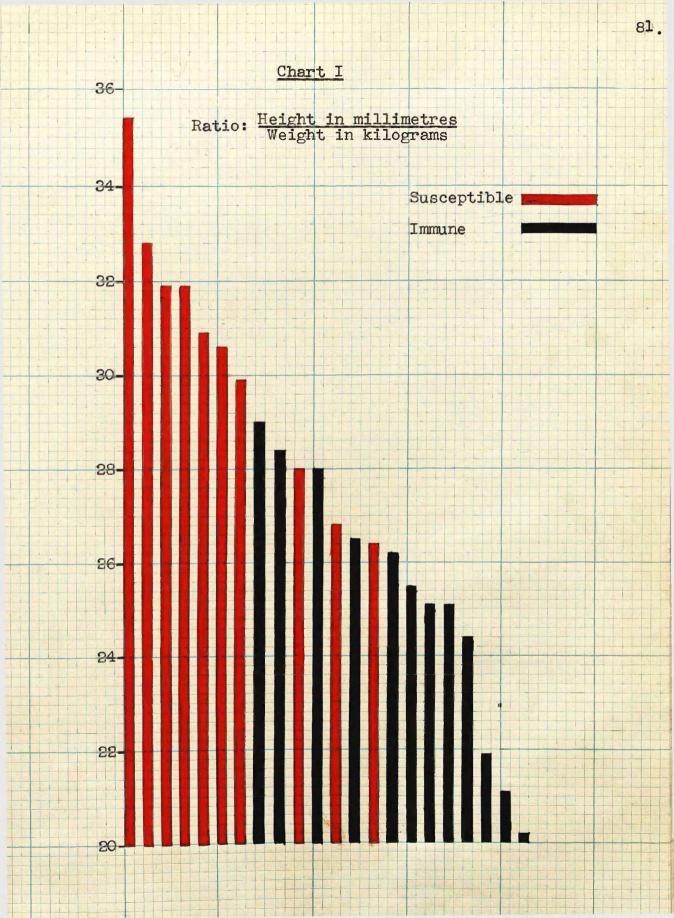
	Patier		
	Weather calm	Weather rough	Patient Seasick
D.H.	110/72	107/76	121/79
A.B.	128/92	117/70	114/74
F.M.	123/91	112/74	109/71
M.S.	110/71	108/70	112/82
B.T.	103/62	94/63	91/56
M.O.	116/77	106/74	104/69
*	118/80	122/82	-

\* Mean of three immune controls.

#### Table VI

#### Arterial Pressure and Pulse-Rate (1) Before and (2) After O.l gm. Acetylcholin.

Name	Age	Sex	Systolic		Systolic Diastolic		Pulse-Rate	
			1	2	1	2	l	2
N.F.	32	m	142	132	76	74	80	76
F.E.	40	m	122	120	72	72	83	77
N.K.	29	m	120	113	83	76	75	68
K.C.	34	m	114	111	77	77	76	72
D.H.	15	m	117	115	79	78	94	72
M.O.	47	f	124	116	82	77	78	72
E.J.	30	f	112	112	72	70	80	74
M.S.	28	f	114	112	74	73	90	87



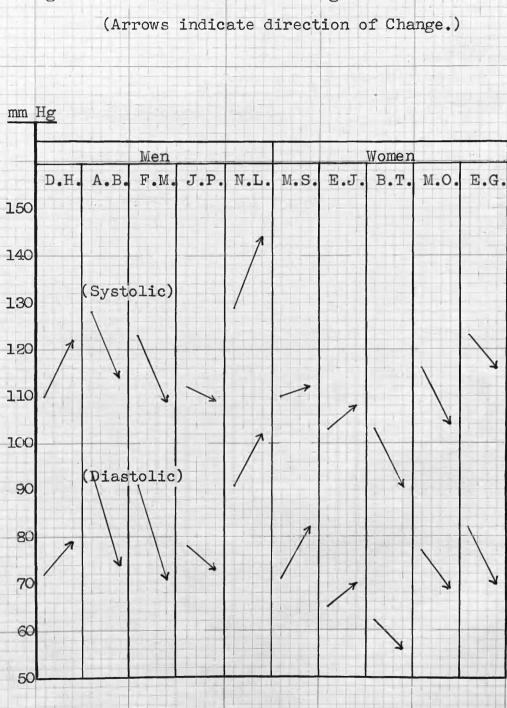


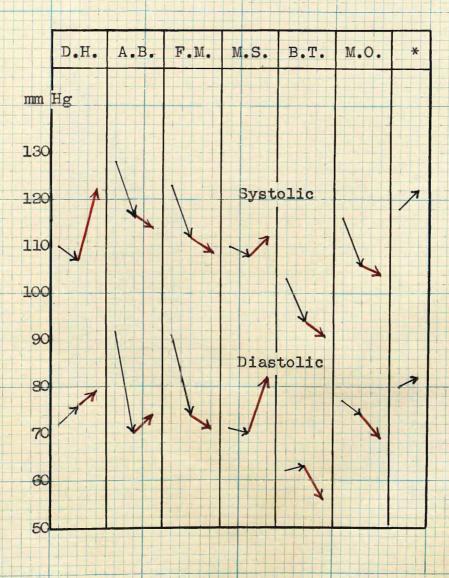
Chart II

Changes in Arterial Pressure during Seasickness.



Arterial Pressure Changes in Rough Weather, Before and After Onset of Seasickness.

Black arrows indicate the change from normal to the conditions found in rough weather without <u>symptoms</u>. Red arrows point to readings taken during actual seasickness.

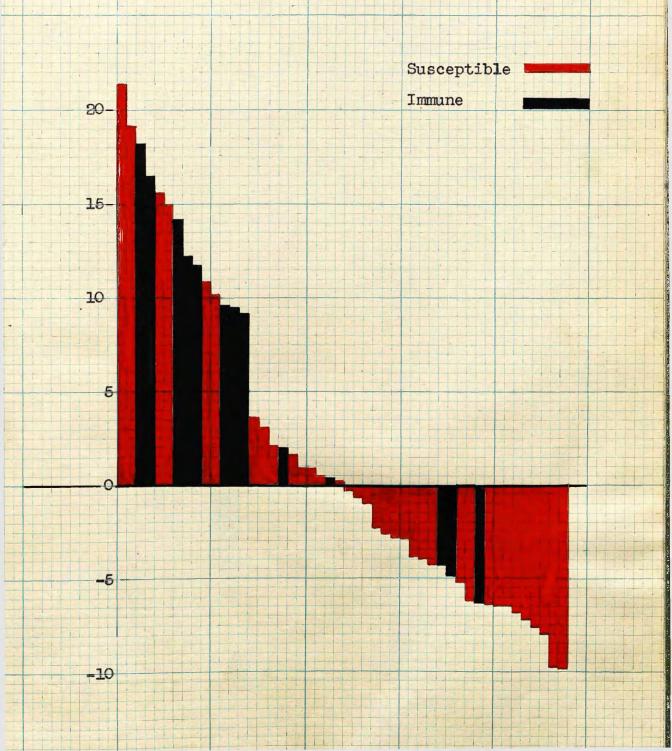


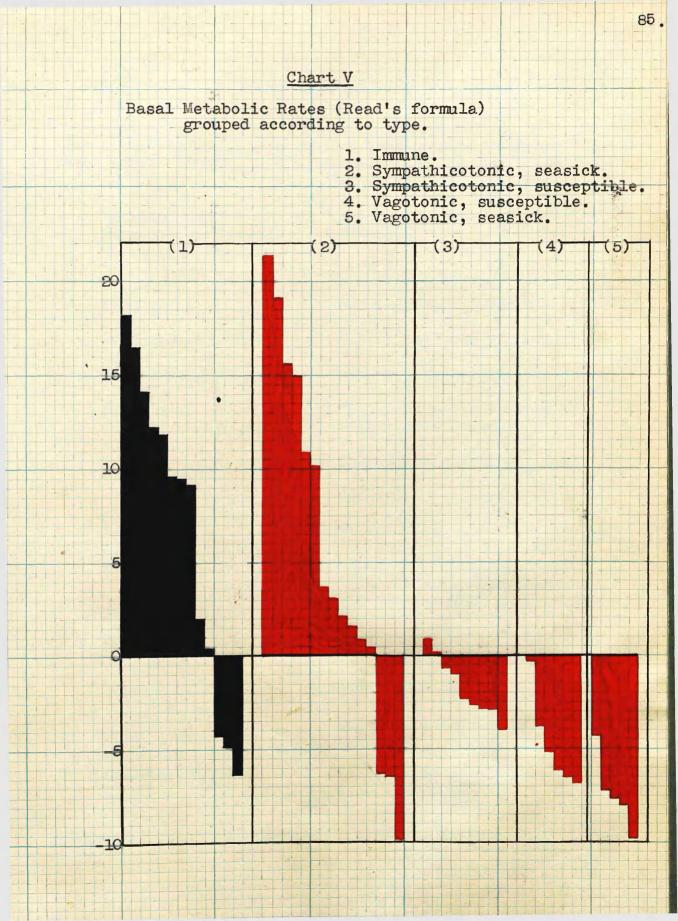
\* Mean of three immune controls.

Chart IV

Basal Metabolic Rates

according to Read's formula.





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References to current medical literature are detailed in the text.

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