EXPERIMENTAL INVESTIGATIONS ON SEASICKNESS

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Aan de nagedachtenis van mijn vrouw

VOORWOORD.

Gewoonlijk vormt een proefschrift de afsluiting van een Universitaire studie. Echter, toen mijn opleiding tot specialist in 1934 was beëindigd, vestigde ik mij te Rotterdam, waar al spoedig de praktijk mijn tijd volledig in beslag ging nemen, waardoor er voor het bewerken van een dissertatie voorlopig geen tijd beschikbaar bleef. Desondanks liet het onderwerp „de zeeziekte", waarvoor ik steeds een levendige belangstelling had gekoesterd, mij niet los. Die belangstelling werd nog versterkt door de vele contacten met de scheepvaart en de zeevarenden, die in deze dynamische wereldhaven ontstonden, doch is vooral voortgesproten uit de nimmer aflatende suggesties, mij gedaan door mijn zeergewaardeerde leermeester Quix, wiens wetenschappelijke verdiensten ik met het klimmen der jaren steeds beter ben gaan begrijpen en steeds meer heb kunnen hoogschatten.

Het is mij een behoefte hier in dankbaarheid te gedenken mijn niet meer in leven zijnde Ouders, die mij in staat hebben gesteld mijn positie in deze maatschappij te verwerven.

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wereld algemeen als zodanig wordt erkend en welk een hoog aanzien U overal geniet. Ik prijs mijzelf dan ook gelukkig, dat Gij bereid waart Uw medewerking aan dit onderzoek te verlenen. De gemeenschappelijke zeereizen, tijdens welke de onderhavige experimenten werden verricht brachten mij tot een erkentelijkheid, welke spoedig in het gewaad der vrienschap werd gekleed. Ook Uw medewerkers van het labyrinthologisch laboratorium wil ik gaarne in deze dank betrekken.

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CHAPTER I

INTRODUCTION: DEFINITION OF PROBLEMS

Man is by nature a land dweller. Although he lives in a three-dimensional world, his movements are still mainly two-dimensional, over the surface of the Earth. He has never been able to do anything else, for throughout his phylogenetic development he has always been bound to the land. Man lives on a planet to which he is bound by a great many factors. His whole existence depends on the Earth's crust on which he is born, from which he derives his existence and to which, after his death, his mortal remains are returned. The analytical psychology of the school of JUNG has demonstrated that the archetype of Mother Earth is engraved in the unconscious of man. For our ego it is of little importance that according to modern physics and astronomy the Earth is not the centre of the Cosmos. Psychologically the Earth is the centre for man. This emotional evaluation is of far greater importance for man than the intellectual knowledge, which can no longer accept this standpoint. For him the seemingly immobile Earth is the base of his position and his movement. It is the static factor, the *terra firma*, to which he is unbreakably bound in his subconscious; this can, for example, be observed in an earthquake, when all of a sudden this fundamental certainty gives way, and the result may be such a drastic interference with this binding that panic breaks out. This becomes first manifest in a general feeling of uncertainty, an undefined sensation of fear, followed by a panic flight; these reactions are apparently innate, as the whole animal kingdom reacts in a similar way.

Man's mind is centred on the Universe, but physically he is bound to a particular spot on the Earth at a certain time. All changes in the relationship of man to space stir the deepest roots of his being. Man

has adapted himself to his surroundings and adjusted his life to distance and space. Technique, however, has conquered distances and cast man into the maelstrom of an era in which, with the aim of conquering space, he has violated his own philosophical and physical stability.

When man's movements on the Earth are analysed in detail, particular attention being given to walking, it appears that he tries to keep his head as far as possible in a constant state of acceleration. This can also be observed in animals. In a trotting horse the irregular movement of the body is intercepted by a compensating mechanism of the neck, so that the head can maintain rectilinear movement. A flying duck also makes use of these compensatory movements of the neck, so that its head continues in rectilinear movement, while its body moves shock-wise up and down owing to the reaction forces of the flapping wings. The tendency to equalization of the movements of the head can be excellently observed in a sufferer from headache: such a person places his feet in such a way that his centre of gravity remains practically at the same level during walking, so that his head, with the help of some other corrections by the trunk, has a practically horizontal rectilinear uniform movement. Man and animals are continuously subjected to the acceleration due to gravity. In their movements, animals evidently always try to attain a condition of constant acceleration. The forces thus provoked in the animal (weight of organs, etc.) are compensated by the animal itself. The animal is used to this simple state of compensation. It also has its adaptations for not quite constant conditions of force. A person walking normally causes with every step a significant change in the vertical acceleration which acts on the body and thus also on the head. While the sufferer from headache counteracts these changes of acceleration, a person normally walking is also able to adapt himself to them. The movements which he has used since his creation take place in a horizontal plane, and he keeps the vertical deviations from this as small as possible, and compensates for them by means of an adapted central nervous system. Walking, being one of the oldest forms of human movement, has in the central nervous system a complete neural mechanism for regulation and coordination.

Other forms of movement, however, will not readily be intercepted

by suitable automatic mechanisms, and this may lead to difficulties in dealing with these unusual forms of movement. The movement of a ship is an important example of the group of uncommon movements which eventually lead to motion sickness.

The physical band with the Earth is localized physiologically in three sense organs, namely the vestibular organ, the visual organ and the proprioceptive system. The orientation, coordination and regulation of these sense organs are indispensable for the maintenance of equilibrium. In his monograph on seasickness DE WIT (1953) has established that the organ of equilibrium of man is undissolubly connected with the 'inertial system' of the Earth. The main function of the organ of equilibrium is at all times the giving of information as regards the position of the head and its movements with respect to this inertial system. When man is forced to leave this safe inertial system there is a great chance that he will react abnormally in his new surroundings. Man's balance is maintained by cooperation of the vestibular system and the proprioceptive system, while, if necessary, the aid of vision may also be called in. In the struggle to maintain himself, man was forced in very early times to take to the sea. There he was exposed to conditions to which he was not physiologically adapted. The essence of these changed conditions is that the surface of the sea is not a stable one, but is more or less continuously in movement, so that the sailor is continually subjected to changing movements. In this way he is exposed not only to the force of gravity, but also to continually changing accelerations in a vertical direction. These continual changes of acceleration must therefore be considered as the essential criterion of the physiologically abnormal conditions obtaining at sea. The human being will react to this in an intrinsically human way. Only by habituation can he succeed in overcoming and suppressing the effects of the action of the undulatory movements on his organs. This is not always possible, i.e., when the sea is too rough or when his bodily condition is subnormal; in this case he pays a toll for being in a situation which is not his natural environment, and he becomes seasick. Moreover there have always been persons who never get accustomed to the movement of a ship at sea. They always become seasick and they remain so until the movement stops.

Seasickness has since early times been a subject of discussion and

investigation. The seasickness problem became very urgent during the second World War, when it was absolutely necessary to transport large bodies of troops in battle condition over the oceans. New anti-seasickness drugs were diligently sought for, because those already existing were unsatisfactory. At the same time a first effort was made to study the quantitative relationship between the ship's movement and the average occurrence of seasickness on board. The results of these experiments were rather vague, but it appeared that the anti-seasickness drugs are far from perfect.

The seasickness problem is an urgent one, especially in the last few decades with the continuous progress of science and technique, resulting in intensified transport. Seafaring is necessary more than ever, and in The Netherlands, as a small seafaring country, this is a vital necessity. Workers in technical and other spheres are seeking means to make travel over the seas more efficient and more comfortable.

In recent years, investigations on non-stationary movements of a model ship have been carried out in the shipmodel basin of The Netherlands Seakeeping Research Laboratory in Wageningen. In these experiments the undulatory movement of the ocean is imitated as far as possible. The DENNY-BROWN automatic gyroscope-regulated stabilizer, developed in England, is already an important improvement, as it actively counteracts the rolling of passenger ships, so that this has now practically been abolished.

Although the rolling of the ship is not the main cause of seasickness, this invention has already contributed a great deal to the increase of comfort at sea.

Medical scientists have also been busy in this field. In the English-speaking countries in particular, a great deal of work has been done in this respect during and since the second World War, as shown in the very great number of publications. This is the main reason why the present work is also published in English.

The small seafaring nation of The Netherlands has furnished a relatively great number of scientific workers in this field. Important papers on this subject have been published by QUIX, VAN EGMOND, GROEN, DE WIT, and others.

However, our understanding of the essence of seasickness is far from complete, and such understanding is of course a primary

condition for approaching the ideal of a reasonably effective method of combating this evil. The following pages deal with an investigation in this field, and we hope that the results will bring us a small step further in the desired direction.

It is not only interesting from a scientific point of view but also of practical value to study the quantitative relationships between the movements of the ship and the course of the seasickness, and at the same time to observe its signs and symptoms more precisely. The activity of some anti-motion sickness drugs can also be evaluated. We are grateful to the Holland-America Line and the Royal Dutch Navy for their kind cooperation, thanks to which the necessary measurements could be carried out on large ships at sea with many people on board, while, by means of questionnaires, the necessary data could be collected regarding the reactions of these people.

We have indeed succeeded in acquiring some improved understanding of the nature of seasickness from a statistical analysis of the questionnaire material, and the corresponding measurements of acceleration.

CHAPTER II

HISTORICAL SURVEY

Seasickness is as old as seafaring. However, it is only rarely mentioned in the writings of the Greek and Roman authors. The reason of this seemingly slight interest has been attributed to the relatively calm nature of the seas sailed by the Ancients. Occasionally, however, something is found of it in the legends. Seasickness overtook ULYSSES and his companions in the Homeric saga. HIPPOCRATES pointed out that when a hellebore draught was administered to a patient to provoke emesis, the patient 'should move about as little as possible and sleep and rest as much as possible'. This advice was based on his conception that 'sailing the seas upsets the body'. Since the word *nausea* was derived from *naus*, the Greek word for vessel, it at first only meant seasickness, but eventually it came to mean an urge to vomit due to other causes as well. CICERO, the Roman statesman, said that he 'would rather be killed than suffer again from the tortures of *nausea maris*'. SENECA and CICERO were sensitive to seasickness, as was JULIUS CAESAR. LIVY reports the following in his description of the second Punic war (218-201 B.C.) ': . . . . and when SCIPIO had noticed that HANNIBAL also thought of crossing the Rhone, he, SCIPIO, still uncertain of the spot on which he would meet him, and while his soldiers had not yet quite recovered from the shaking to and fro at sea, sent 300 picked horsemen with guides from Massalia (the present Marseilles) in advance to reconnoitre'.

Of Lord NELSON, the famous hero of Trafalgar, it is reported that during his whole career he was always seasick except when he had to fight a battle.

It is not surprising that in the course of time many opinions have been put forward and many theories evolved to explain the nature

of seasickness. The historical study of these theories is highly interesting because they are true reflections of the often fantastic ideas which alternated and conflicted with each other in the physiology and anatomy of former times.

The following are some of these theories.

1. Labyrinthine theory: The upset is caused by overstimulation of the organs of equilibrium in the internal ear, resulting in overflow of stimuli to other centres and to the vagus nerve.
2. Confusion resulting from the multiplicity of unusual stimuli to sensory nerves, caused by adjustment of the position of the body in space.
3. Eyestrain caused by the glare of sea and sky, and the unusual fixation upon moving objects, has also been advanced as a cause.
4. The wide excursions of the freely movable organs of the abdominal cavity may cause overstimulation of the vagus nerve.
5. Autosuggestion.
6. Acidosis.
7. Neurological theories of vagotonic and sympathicotonic types.
8. Visceroptosis.
9. Movements of the ship.

WILLIAM HYDE WOLLASTON (1766—1827), the eminent ophthalmologist, famous for his researches on the physiological mechanism of central vision, being impressed by the oscillations produced in the mercury of a barometer by the up-and-down movements of a ship, propounded the theory that the blood in the vessels behaved in a similar fashion and so caused an alternate engorgement and ischaemia of the brain. Even until quite recently (1957) this idea has had its adherents.

Two groups of explanations are in general to be distinguished, viz. the group of the non-mechanical and that of the mechanical theories. The latter have found the greater number of adherents because the relationship between the ship's movements and the pathogenesis of seasickness is so very spectacular. When the sea is smooth and the ship lies quite calmly on it, seasickness does not arise, and conversely. There are more victims the rougher the sea.

The movements of the ship are transmitted to all parts of the body, and thus almost all organs in their turn have been regarded as the starting point of seasickness. In the first place, of course,

came the stomach, because the gastric symptoms predominate in the clinical picture of seasickness. Next the liver, the heart, the blood, the brain, the cerebrospinal fluid etc. were thought of; practically no part of the body was forgotten, and even in our own times we may hear in conversation with non-medical but often well educated people, for example during a sea voyage, all kinds of most peculiar theories on seasickness; the best thing one can do is to answer them with a polite smile.

Even the Greeks suspected that seasickness might have some relationship to the organ of hearing. FLOURENS, famous for his operations on the semicircular canals in pigeons, was (in 1824) one of the first to point out that seasickness might be caused by the effect of the ship's movements on the organ of equilibrium, which, together with the organ of hearing, was situated in the petrous bone. On anatomical examination of the petrous bone, the three semicircular canals with their mutually perpendicular positions in space, formed such a striking feature that each investigator in turn came under the impression of this geometrical wonder. This may explain why the three semicircular canals were always regarded as the most important part of the organ of equilibrium, and it was not until comparatively recently, in 1873—1874, that the difference in function between these canals and the otolith organ was realized. In this period MACH, BREUER and CRUM-BROWN, independently of each other but at about the same time, made a distinction between the two parts of the organ of equilibrium.

In 1875 BREUER, who repeated the experiments of FLOURENS, described the difference in function between the semicircular canals on the one hand, and the otolith organs on the other. He regretted that he had been unable to remove the otoliths or to stimulate the otolith organ without causing damage to the surrounding tissues. He attributed the positional reflexes to the otoliths, and arrived at the conclusion that the labyrinth is the sense organ that can perceive rotation by means of the semicircular canals, while the linear movements and the position of the head in space are perceived by means of the otoliths.

MACH, who was a physicist, showed that it was not uniform movement, but accelerated movement that had to be regarded as the stimulus to the organ of equilibrium.

KREIDL's classic experiment which consisted of substituting iron filings for the ordinary sand otolith in the prawn, showed that movement of the iron otolith by a magnet caused a marked disturbance of the animal's equilibrium; this suggested that it is the pressure of the otolith on the haircells which acts as a stimulus. After bilateral labyrinthectomy, frogs, pigeons, guinea-pigs and dogs no longer show any reaction to progressive movements or linear acceleration. Similar results have been reported by ACH, BROWN, MAGNUS and DE KLEYN, FISCHER, TAIT and MCNALLY, BENJAMINS and HUIZINGA and SJÖBERG.

In 1896 JAMES stated that deaf mute persons did not become seasick.

BROWN, MAGNUS and DE KLEYN and VERSTEEGH concluded from their experiments that linear or progressive movements may stimulate the semicircular canals. The whole canal is presumed to be displaced with respect to the crista, by inertial forces. In this case it would be possible for a crista to be stimulated without the intermediary of the cupula. This will presumably only be the case with extreme stimulation.

The weight of the experimental evidence is, however, in favour of the otolith organs being the organs most stimulated by linear accelerations. This opinion is supported by BREUER, MACH, EWALD, LEE, ACH, WOJATSCHEK, BÁRÁNY, MCNALLY and TAIT and HASEGAWA.

MAGNUS and DE KLEYN and EWALD stated that there is no ocular nystagmus in response to linear acceleration. GROEBBELS and also TAIT and MCNALLY have reported that after elimination of the semicircular canals, normal reactions can still be elicited in response to linear acceleration. According to TAIT and MCNALLY, after bilateral removal of the saccule and the utricle in a frog, the semicircular canals did not show any reaction to linear acceleration.

The experiments of BÁRÁNY, SJÖBERG and WOJATSCHEK indicated that the chief disturbing factor in the pathogenesis of motion sickness is the vertical linear acceleration, and, as previously pointed out, this movement stimulates the utricle.

In 1931 QUIX, in collaboration with the mathematician WERNDLY, carried out a theoretical analysis of the movements of a ship on the waves of the sea, calculating the angular and linear accelerations

resulting from these movements. It appeared that the angular accelerations usually did not exceed the minimum perceptibile of the semicircular canals, while the vertical linear accelerations attained values much higher than the minimum perceptibile of the otolith organs. The author of the present study has arrived at the same conclusions, but now on the basis of direct measurements of angular and linear accelerations aboard the 'Maasdam'.

As far back as 1875 BREUER contended that the action of the otolith organs must be based on a sliding of the otolith over the macula. Later this theory was disputed by various workers, including QUIX in 1903 and RUYSCH in 1909. It was then thought that, under the influence of an acceleration, the otolith pressed more or less on the macula. QUIX called this the 'pressure' of the otolith. There were others who were more in favour of a 'traction' of the otolith. There was even some controversy between the advocates of the 'pressure' and 'traction' theories.

QUIX was of the opinion that with the subject in the supine position, there was a certain position of the head in which neither the sacculus otolith nor the utricle otolith was able to exert its pressure on the macula. He called this the 'blind spot' of the otoliths. He also made a therapeutic application of this by advising the seasick person to lie flat on his back with his otoliths in the 'blind spot'. He even designed an apparatus with a counterpoise, suspended in gimbals, by which the patient was kept in the so-called blind-spot position of the otoliths. The anti-seasickness cushion of UTERMÖHLEN seems to be based on the same principle. In practice, however, these devices were not satisfactory.

In 1955 a paper on the structure of the macula utriculi was published by WERSÄLL, ENGSTRÖM and HJORTH. The sliding theory of the otolith returned to favour again in 1950 when HESSEL DE VRIES proved experimentally that the otolith could be displaced in a direction parallel to the macula.

The otolith organ must be regarded as the specific receptor for linear accelerations. Here the nervous apparatus corresponding with it receives its stimulus. These stimuli are elaborated by this nervous apparatus, as will be described in a following chapter.

According to the newest ideas, motion-sickness is an overstimulation syndrome of the vestibular system. The whole problem of

seasickness therefore belongs to the neuro-physiology of the vestibular system.

Actual research on seasickness is relatively young. In spite of recent progress in prevention by drugs, seasickness has remained a pressing problem, especially in a military respect during and after World War II. Both airsickness and seasickness are responsible for reduced efficiency of personnel who may be rendered merely uncomfortable or acutely ill, dependent on the physiological and psychological response of the individual.

TYLER and BARD review the aetiology from the standpoint of the physiological and psychological mechanisms. They state: 'The obvious first step in the determination of the aetiological factors of seasickness should logically be the measurement of those characteristics of motion conducive to sickness'.

MORALES, in an excellent review, analyses the mechanism of the neural responses of the receptors involved which precipitate motion-sickness. He points to the necessity, insofar as seasickness is concerned, of collecting data on the motions of various types of ships in varying seaways as a pre-requisite to any study of the problem.

HANDFORD, CONE and GOVER attempted to evaluate the incidence of seasickness relative to the prevailing motions of the vessel at a given location aboard ship at a given time, but no significant correlations were obtained.

From the preceding we see that the idea of studying the relationship between motion of the ship and the total symptomatology of the resulting seasickness has its justification. The use of anti-seasickness drugs also comes within the scope of this investigation.

CHAPTER III

ANATOMY AND PHYSIOLOGY OF THE VESTIBULAR SYSTEM

The organ of equilibrium, with its communications to the higher centres in the central nervous system, controls and regulates the movements of man and his position in space. It is a highly complicated system of perceptive organs and the corresponding nervous structures, and a good deal is known about its function and its relationship to other parts of the central nervous system — including the autonomic system which is particularly important for our subject.

We therefore prefer to speak of the vestibular system, which can be subdivided into a peripheral and a central part.

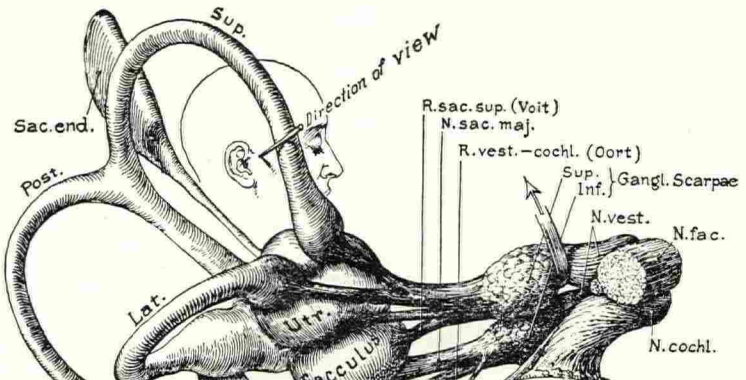


Fig. 1.

The human membranous labyrinth and its innervation. (From HARDY, *Anat. Rec.*, 1934, 59, 403).

1. The peripheral vestibular system

The Vertebrates have in the skull two vestibular organs, situated symmetrically in the superior parts of the labyrinths, which themselves are contained in the petrous bones. The irregularly shaped space left in the bony substance of the petrous bone contains the membranous labyrinth, which, apart from the cochlea, can be divided into:

a. *the utricle,* with the macula utriculi and its otolith;

b. *the saccule,* with the macula sacculi and its otolith.

The utricle is 3.8 mm long and 2 mm thick, while the dimensions of the saccule are 1.5 x 1 mm. In man the otoliths of utricle and saccule are more or less of the same size. Their diameter is about 0.7 mm and their height, measured after fixation, is 0.03 mm.

c. *the three semicircular canals,* all of them originating from and uniting again in the utricle; each of them contains a cupula with crista.

In man the three bony canals are practically of the same size: the diameter is 7 mm for the anterior vertical canal, 6 mm for the posterior vertical canal, and 5 mm for the horizontal canal.

The cross-sectional diameter of the membranous semicircular canals is 0.6 mm; the ampulla, which is here widened with respect to these canals, contains a cupula 1 mm high. The crista is about 0.6 mm high.

These three membranous spaces are in mutual communication, and are filled with endolymph. The membranous labyrinth is surrounded by perilymph and is, at the spot where the nerve enters the sense organ, firmly attached to the bony labyrinth; at many places it is, however, suspended only by strands of connective tissue from the bony labyrinth, so that passage of perilymph is possible.

The whole endolymphatic system, under which must also be included the cochlear duct of the inferior part, is connected via the endolymphatic duct with the intracranially situated saccus endolymphaticus. It thus forms a closed system, without other open communication with the further contents of the labyrinth or even of the cranium.

The plana semilunata are regarded as the sites of production or reabsorption, or possibly both, of the endolymph; further the stria vascularis and the cells situated in the internal sulcus of the scala media: the function of the saccus endolymphaticus in this respect is not yet quite clear. According to GUILD the saccus endolymphaticus is the absorption organ for the endolymph of the whole endolymphatic system. According to BRINKMAN the saccus endolymphaticus possesses a protective function for the rest of the labyrinth.

A membrane in the vestibulum divides the perilymphatic space into two parts: the *pars superior* containing the three semicircular canals and the utriculus and the *pars inferior* containing the cochlea and the sacculus.

The perilymphatic system of the pars inferior is in communication with the subarachnoid space via the cochlear aqueduct. The pars superior is also in communication with the subarachnoid space; this communication takes place via the bony canal surrounding the endolymphatic duct.

The composition of the endolymph is essentially different from that of the perilymph, especially with respect to the K and Na ion concentrations in mEq./l. (NACHMANSOHN).

	Perilymph	Endolymph	Blood	Cerebrospinal fluid
Na^+	153.7	15.2	138.6	154.8
K^+	4.77	137.7	4.79	4.82

The very high potassium content of the endolymph shows that the nervous communications must run entirely in the perilymphatic system: any contact with the endolymph would instantaneously stop the transmission of information in the form of action potentials (TASAKI, DAVIS and ELDREDGE, 1954).

Anatomically there is a great resemblance between the macula with its otolith and the crista with its cupula. Both contain sensory epithelium (ENGSTRÖM, WERSÄLL), consisting of at least two types of sensory cells (types I and II of WERSÄLL). Supporting cells lend great firmness to both structures. All the sensory cells bear cilia: these penetrate into otolith and cupula. The sensory cells differ in the way in which the dendrites of the neurons make contact with the cell body (WERSÄLL). The apex of the crista contains mainly sensory cells (type I), the bodies of which are almost completely situated

within a chalice-shaped mantle consisting of dendrites with their buds. These cells are presumably the transmitters of the special information given by the semicircular canals, i.e. about the rotatory movements of the head. The type II sensory cells are mainly situated at the basis of the crista; the remarkable feature of this type II cell is that the contact between the dendrites of the neuron and the cell body is simpler and less extensive than in the other type; the cell

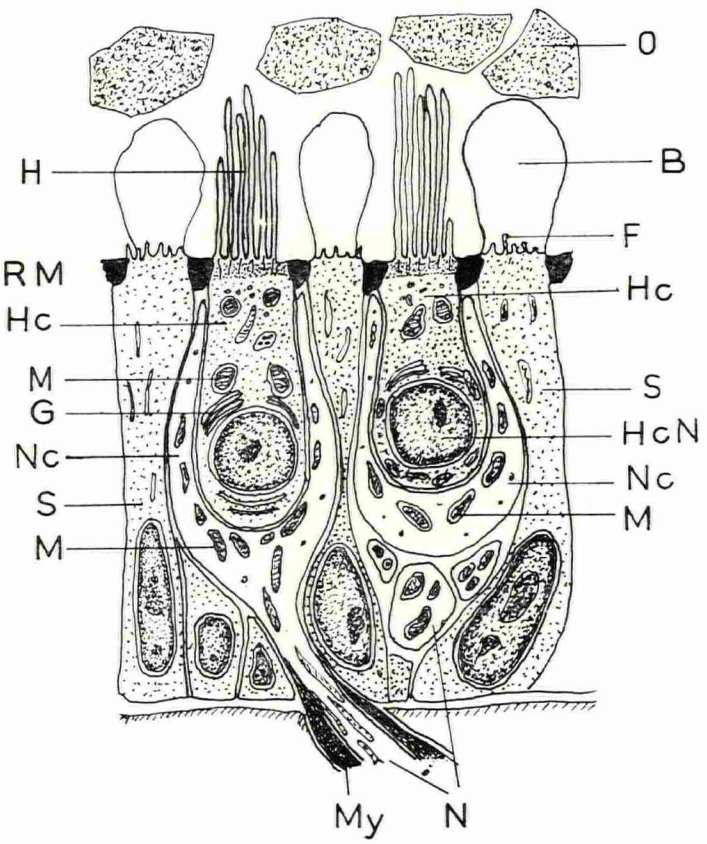


Fig. 2.

Schematic drawing of a guinea pig macula with otolith. N nerve, with nerve chalice Nc. Hc sensory cell. H cilia on haircell. RM reticular membrane. B balloon-shaped and F fingerlike processes. S supporting cell. G Golgi apparatus. M mitochondria. HcN nerve cell nucleus. O statoconia. My myelinated sheath. (WERSALL, ENGSTRÖM and HJORTH. Suppl. *Acta Oto-Lar.* 114—117 page 302).

has a more cylindrical form and the contact between buds and cell takes only place against the bottom wall. The cells of type II might be regarded as remnants of a much older structure of ciliated epithelium, as still found in active form in the labyrinth of *Petromyzon* (the lamprey).

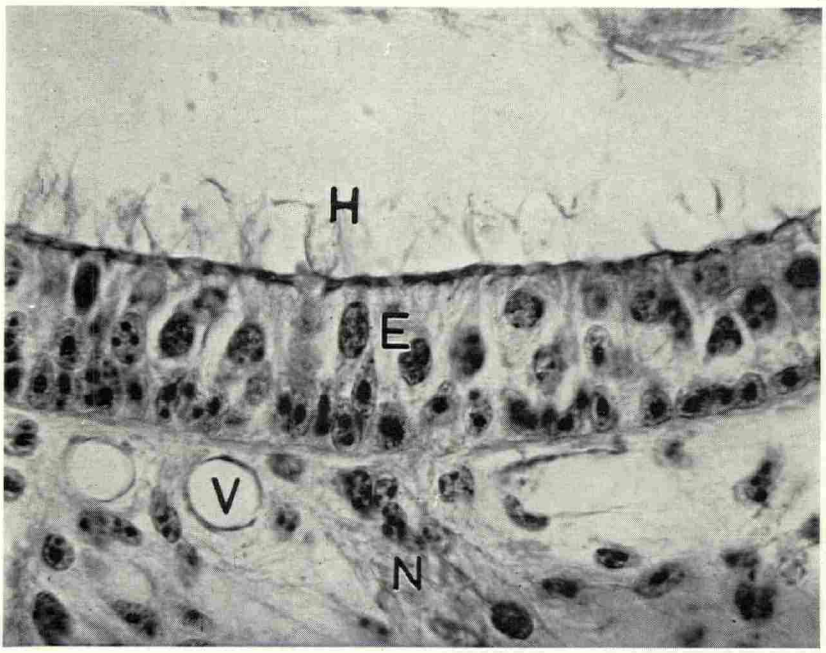


Fig. 3.

Section through the utricular macula in guinea pig. N nerve; V vessels; H hairs on the macular surface; E macular epithelium. Magnification (linear) 1000 x. (WERSÄLL, ENGSTRÖM and HJORTH, Suppl. *Acta Oto-Lar.* 114—117 page 302).

There is a small but important space between cupula and crista and between macula and otolith. Both structures, cupula and otolith, can slide over their respective bases, the crista and the macula, and this is of fundamental importance for the function. Cupula and otolith differ in the following respects:

a. Density. The cupula is of the same density as the endolymph surrounding it. Linear accelerations therefore do not exert any influence on it. The density of the otolith is determined by the

aragonite crystals present within its membrane. The difference in density between otolith and its surroundings is what causes the otolith to react to linear accelerations.

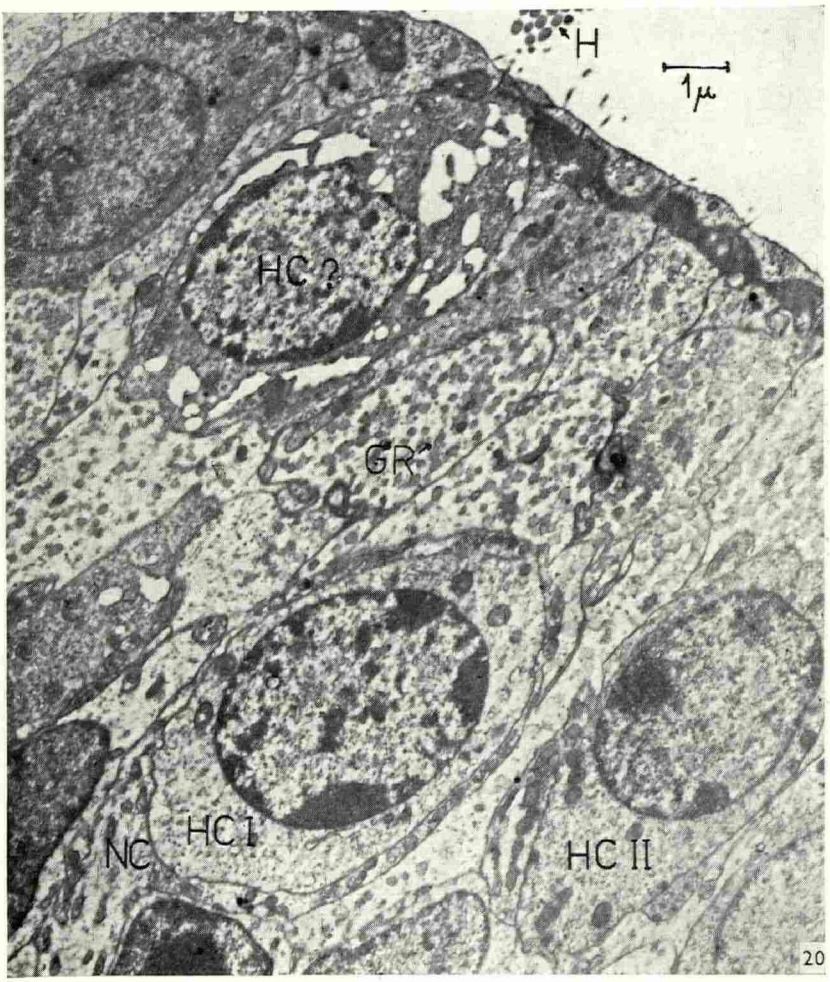


Fig. 4.

Section through the sensory epithelium of the macula utriculi in guinea pig. NC: nerve chalice. HCI: haircell type I. HCII: haircell type II (WERSÄLL 1956). GR: granules in a supporting cell. H: cross section sensory hairs. HC?: haircell with vesiculated cytoplasma.

(ENGSTRÖM and WERSÄLL, Suppl. V *Exp. Cell Research* 1958).

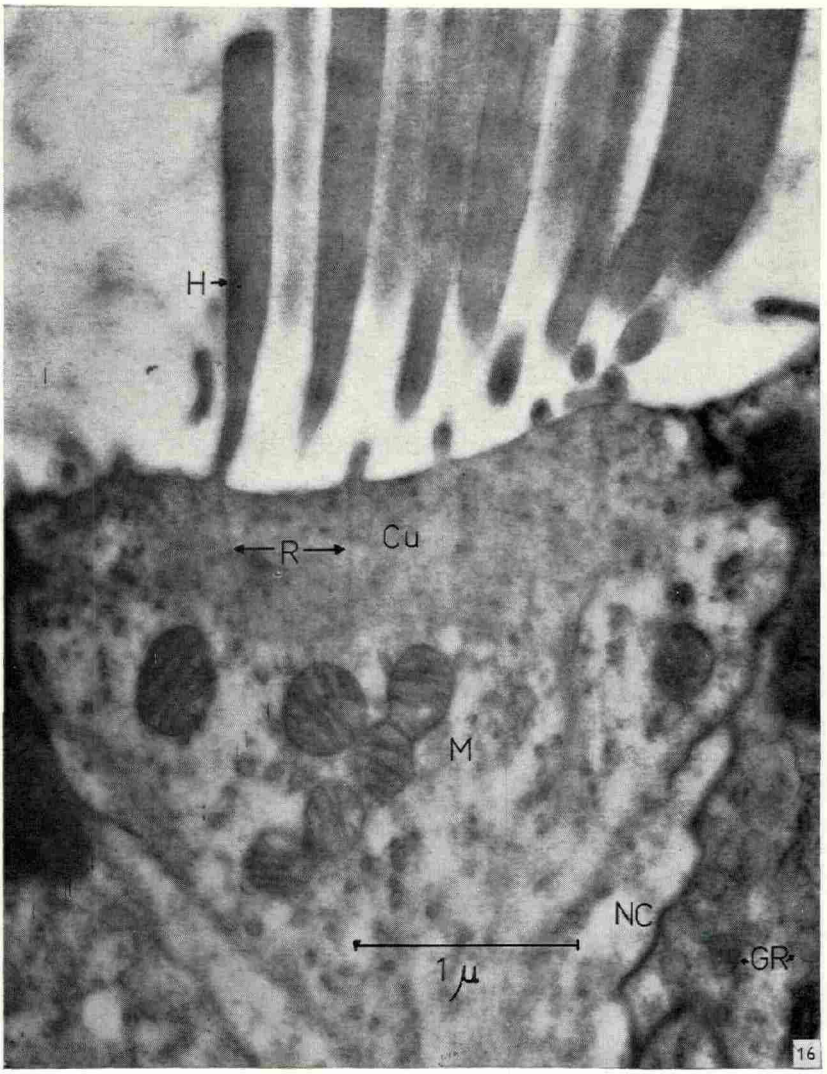


Fig. 5.

Upper part of a haircell of type I. H: sensory hair with axial fibril passing down into the cuticle (Cu) as a thin rootlet (R). M: mitochondria. NC: nerve chalice. GR: granules in a supporting cell.
(ENGSTRÖM and WERSÄLL. Suppl. V *Exp. Cell Research* 1958).

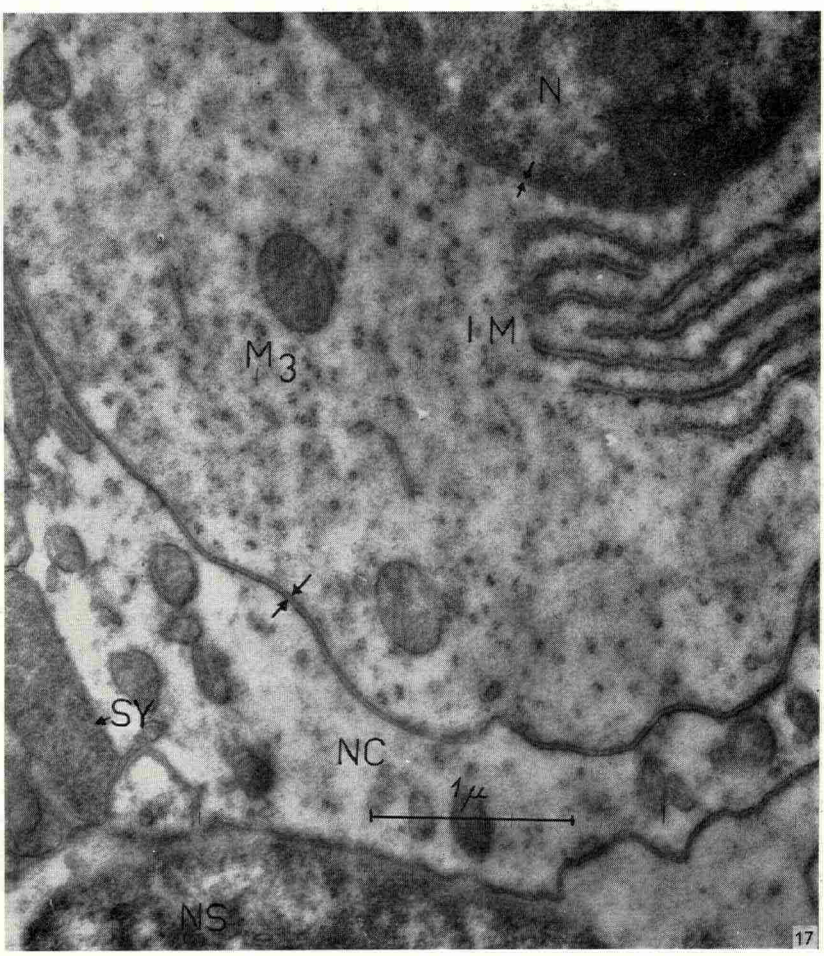


Fig. 6.

Lower part of a haircell of type II with surrounding nerve chalice (NC) and a synaptic nerve ending (SY) in close contact with the nerve chalice. Under the nucleus (N) is found a system of granulated membranes (IM). M3: mitochondrion. NS: supporting cell nucleus.
(ENGSTRÖM and WERSÄLL. Suppl. V *Exp. Cell Research* 1958).

b. Suspension. The cupula is a soft gelatinous structure, extending from the crista to the roof of the ampulla and hermetically closing

the latter (STEINHAUSEN, DOHLMANN). The cupula is elastically attached at the basal sides of the crista. The slightest displacement of endolymph in the canal causes a shift and bulging out of the cupula with respect to its crista. The otolith, which is comparable with a 'heavy' cupula, is firmly attached to the lateral walls of the macula. The displacements of the otolith are therefore very small 0.1—0.2 mm for accelerations in the order of g (10 m/sec^2) (HESSEL DE VRIES, 1950).

c. *Natural period.* The flaccid cupula is forced by the endolymph into every position that is imposed on the latter by the rotatory inertial forces. The cupula itself returns again slowly to equilibrium position, pushing the endolymph through the narrow semicircular membranous canal (0.6 mm diameter and about 10 mm long). Because of its elastic properties (slight though these are) and its coupling to the endolymphatic fluid ring, it behaves as a torsion swing with a natural period of 6 seconds (VAN EGMOND, GROEN and JONGKEES).

The fact that this system possesses a natural period does not imply that it can swing freely, because the cupula is 'creepingly damped' owing to the marked friction of the endolymph in the narrow canal. The otolith reacts much more quickly than the cupula when it has to assume its equilibrium position on its own account. VON BÉKÉSY measured values of 0.1 to 0.05 seconds in man, while DE VRIES (1950) found 0.02 to 0.005 seconds in carp-like fishes.

In the above description of the suspension and the natural period belonging to it, it is assumed that the otolith slides over the macula, but it must be pointed out that this sliding never takes place over distances which are of the same order of magnitude as the otolith itself. The sliding theory, originally formulated by BREUER (1874), has later been disputed by various authors, for example by QUIX (1903) and RUYSCH (1909). RUYSCH experimented with X-ray technique in sharks, and tried to ascertain by placing preparation and X-ray apparatus together in different positions, whether the otolith was displaced with respect to the other parts of the head. As his measuring technique did not allow a precision greater than 0.1 mm., he failed to demonstrate the displacement. It is interesting to mention here that DE VRIES (1950), with a similar technique, did

succeed in clearly demonstrating the displacement in carp-like fishes, thus corroborating BREUER's hypothesis. ULRICH (1935) also demonstrated the sliding as an essential movement in the pike. He showed in the living preparation that reactions only arose when the utricle was displaced with a stiff hair in different directions. A forward and lateralward pressure of the hair caused changes in position of the eyes on the homolateral and contralateral sides, in such a way that the eyes moved in opposite directions. Displacement of the otolith to the medial side had no effect at all. The utricular otoliths thus act synergistically, the left otolith regulating the compensatory eye movements with rotation around the longitudinal axis to the left, while with rotation to the right the right otolith comes into action.

Many of the above data have been provided by LÖWENSTEIN and his collaborators SAND and ROBERTS. It may be worth while to mention that these authors studied also a special part of the macula of utriculus and sacculus, a part which does not react to slow changes of linear acceleration but exclusively to vibration. In the utricle this is a part of the macula which is not covered by an otolith; it is called the lacinia. The posterior part of the sacculus macula also reacts only to vibration (LÖWENSTEIN, ROBERTS). Thus we find ourselves involved in the old controversy about the function, which will be discussed further below.

For the sake of completeness we must mention here the presence in the labyrinth of a type of sensory cell corresponding to type II as found in the outer hair cells of the organ of Corti. In contrast to the inner hair cells and the vestibular type I, these cells are also cylindrical of form with a firm wall. They are therefore comparable with a closed cylinder, the lid of which bears the cilia and the bottom of which is thin; the buds of the dendrites lie closely packed against the bottom. In contrast to the preceding structure, in which the cell is, as it were, completely embedded in the dendrites, this structure suggests that, during the 'stimulation phase', the wall of the sensory organ must be permeable to an agent active in transmitting the stimulus information to the nerve. The wall of the cylinder is presumably impermeable, in contrast to the bottom; therefore the dendrites are found only at the bottom, while in the general cell type the whole wall is presumably permeable, and therefore

must be surrounded by the dendrites in order that all active agents may be intercepted.

Function

Many fibrils originate both from the crista and the macula (both possess about 3,000); a large proportion of these fibrils conduct a constant stream of action potentials. Stimulation of the organ leads to change of frequency of these action potentials. The transmission of information from peripheral organ to central nervous system appears to be effected by frequency modulation. Within physiological limits the modulation is proportional to the strength of the stimulus.

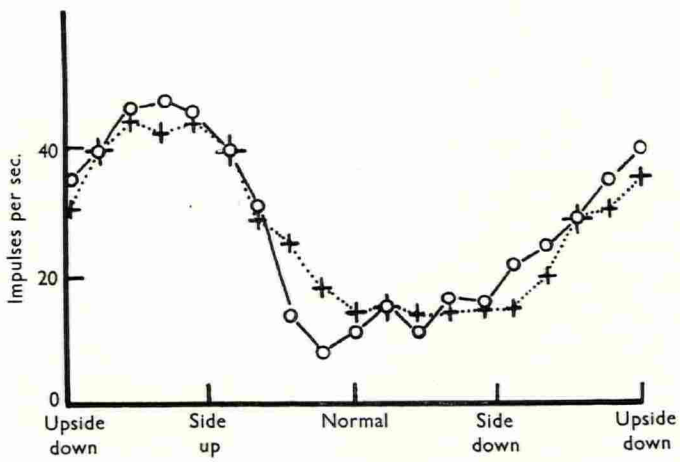


Fig. 7.

Discharge frequencies of the utriculus of *Raja clavata* during two full-circle lateral tilts in opposite directions. The continuous curve to be read from left to right, the dotted curve from right to left.
(LÖWENSTEIN and ROBERTS; *J. Physiol.* 110, 392, 1949).

The experiments of LÖWENSTEIN and ROBERTS on the macula and those of GROEN, LÖWENSTEIN and VENDRIK on the crista provided the data mentioned above. Fig. 7 is borrowed from the work of these authors.

This figure shows how, in a single fibre preparation from the

utricular nerve of *Raja clavata*, the frequency of the action potentials is measured as a function of the position of the head. This figure represents a rotation of the animal around its longitudinal axis. Fig. 8 gives a registration of the same fibre, but now for a rotation around the transverse axis of the head.

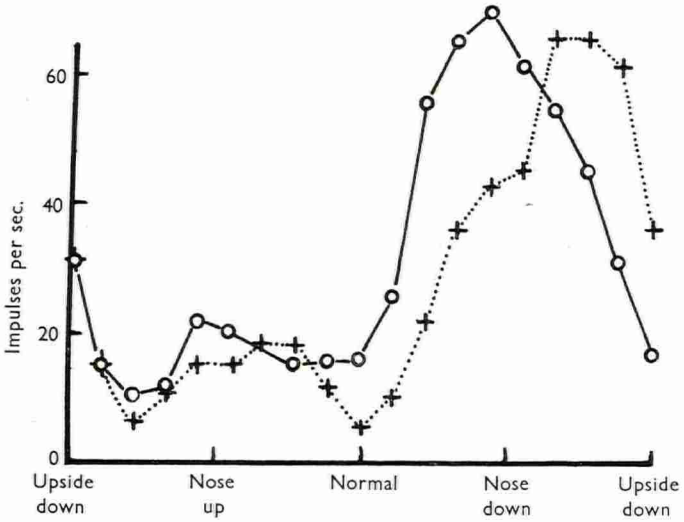


Fig. 8

Discharge frequencies of the utriculus of *Raja clavata* during two full-circle fore-and-aft tilts in opposite directions. The continuous curve to be read from left to right, the dotted curve from right to left.
(LÖWENSTEIN and ROBERTS; *J. Physiol.* 110, 392, 1949).

In the first place it is shown that the utricle reacts to changes of position of the head in all directions. Secondly, there is a certain lag (hysteresis), as appears from two measurements for one particular position of the head, obtained by making two rotations in opposite direction. It is also shown that the frequency of the action potentials for a given head position depends on the duration. If, for example, in the beginning the nose-up position yielded 16 discharges per second, this rate fell to 11 per second after only 30 seconds, and then remained practically constant for the next 20 minutes.

A similar phenomenon was observed by ADRIAN in the vestibular

nuclei of the cat. Hysteresis and adaptation deform the simple picture of a purely stimulus-proportional frequency modulation. Moreover, the increase of frequency is comparatively unlimited, while the decrease of frequency is limited by the value of the basic discharge; the change of frequency in a downward direction can never be greater than is allowed by the value of the resting frequency. Physiologically, this is probably not important for the animal, because the organs of equilibrium are destined to record positional changes with respect to the normal posture, and are not intended to do so for a long time in abnormal positions.

The nerve originating in the crista has a similar nature (GROEN, LÖWENSTEIN, VENDRIK). On slight stimulation of the crista of the horizontal canal, the preparation being placed on a torsion swing with vertical axis, it was shown that the sinusoidal impulse mechanism also caused a practically sinusoidal frequency modulation of the resting frequency (Fig. 9). The phase differences between this curve and the true impulse supplied the data for calculation of the natural period of this preparation.

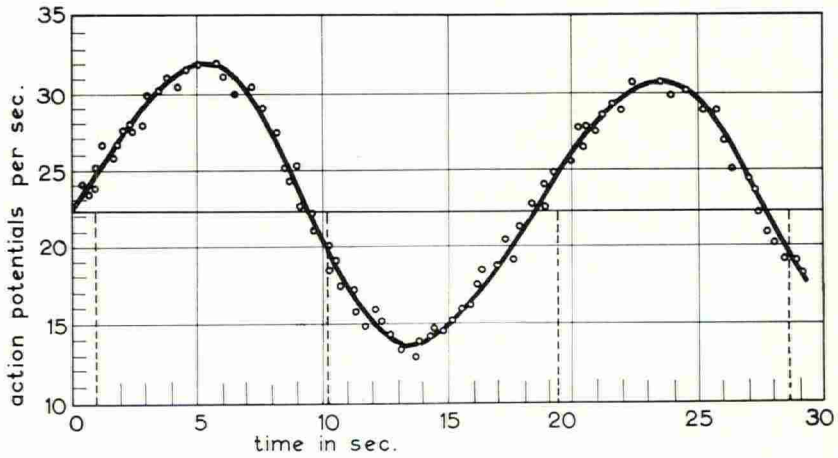


Fig. 9

Discharge frequencies of a single fibre preparation of the ampullary nerve of the lateral canal of *Raja clavata* during a sinusoidal vibration with a period of 18.4 sec. The dotted lines represent the turning point of the swing. The cupula leads by 13.5 ± 2°.

(GROEN, LÖWENSTEIN and VENDRIK; *J. Physiol.* 117, 329, 1952)

Another interesting phenomenon is the great variation in resting frequency. There are fibrils (see Fig. 9) which might be called proportional, because the resting frequency is favourably situated in the whole frequency range of action potentials which can be delivered by this fibril. On the other hand, there are fibrils which give off action potentials only at the moment when the crista is stimulated in the sense of EWALD's positive stimulation; the resting frequency is nil in this case. Other fibrils fire at top speed (200 to 250 discharges) and react only to negative stimulation, in the sense of EWALD, by lowering their frequencies. In this way the whole scale of fibrils between these two extremes is filled, so that it is physiologically possible to transmit the information to the central nervous system over a large intensity range of the stimulus.

The permanent stream of action potentials, which leaves the crista and macula also in rest, is considered to be the tonus-maintaining agency of the peripheral labyrinth on the muscles of neck, body and extremities.

An interesting phenomenon was observed in the above experiments; the peripheral organ of equilibrium does not possess a threshold in the sense of the classical all-or-none law. This latter supposition would lead to the assumption that, with a critical threshold value of the stimulus, action potentials would suddenly be released in the nerve, and that these action potentials would then form the first information about this stimulus. But nothing is further from the truth: as far as the above mentioned authors were able to ascertain within the limits of accuracy of their measurement, no threshold can be measured using the principle of frequency modulation. The threshold will rather have to be defined as the physical stimulus which gives the same frequency modulation as the static fluctuation in the frequency per fibril (averaged over the whole group) would amount to.

Summarizing, we may say that the macula reacts to linear accelerations thanks to the inertia of the otolith; the latter slides over the macula and stimulates the sensory cells, via the cilia, by the shearing forces thus caused; this gives rise to a frequency modulation of the action potentials in the fibrils of the nerve.

A corresponding behaviour is shown by the semicircular canals; in this case it is the inertial force, elicited only by rotation, which

makes the cupula bulge out and slide over the crista. Here also shearing forces arise and, in an analogous way, cause a frequency modulation of the action potentials via stimulation of the sensory cells.

Sensitivity

In man it has been ascertained (monograph of VAN EGMOND, GROEN and JONGKEES) that the threshold for the otoliths is presumably 6 cm/sec^2; this threshold must be of a central origin, in view of the mechanism of the peripheral organ. The task of the otoliths is performed in the range around 1000 cm./sec^2 (the acceleration due to gravity), so that it can be said that these organs possess a very high sensitivity in the range for which Nature made them. The semicircular canals have a minimum perceptible angular acceleration of 0.2° per sec^2, measurable as turning sensation or tendency to nystagmus after about 40 seconds. This long time is necessary because of the slow action of the canal when stimulated with a constant angular acceleration. For impulse-like stimuli the threshold is about 2.5° per second. The majority of physiological movements are rapid with respect to the natural period of the semicircular canal, so that in judging the effect of physiological rotation its character as an impulse activity on the semicircular canal should be taken into consideration. This is done in cupulometry, in which the relationship between stimulus and reaction is measured as duration of sensation and/or duration of nystagmus as a function of the angular velocity just before sudden braking.

Many experiments on the sensitivity to linear and rotatory impulses have been carried out in animals.

Central elaboration of the stimulus

In cupulometry, as mentioned in the preceding paragraph, a phenomenon was found which induced us to include in our considerations the elaboration of the stimuli by the central nervous system.

This phenomenon is the central inhibition, which also constitutes a very important factor in seasickness; this is the reason why we prefer to give first a brief explanation of cupulometry, following which some light can be shed on this inhibition.

Cupulometry

Cupulometry is a refined form of the clinical turning-chair examination. The subject sits on a turning chair or is placed in a turning chamber, with a vertical axis of rotation. All sorts of precautionary measures are taken to ensure the subject does not receive visual, acoustic or cutaneous stimuli, which might give him information about the presence or absence of rotation. The subject is set rotating with a subliminal acceleration until he has reached an angular velocity of the desired magnitude, between 2 and 90°/second, after which the motion is constant and the acceleration therefore zero. The subject notices nothing during the gaining of speed and the final constant rotation. Suddenly (within 2 seconds) he is stopped, so that a negative angular acceleration is imparted

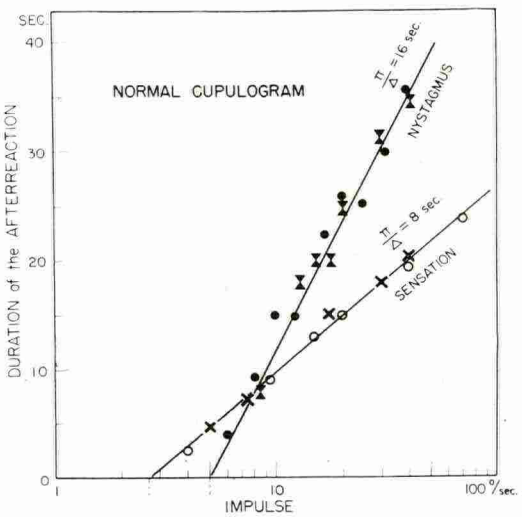


Fig. 10.

Normal cupulograms of sensation and nystagmus.
o sensation after clockwise turning
x ,, ,, counter-clockwise turning
• nystagmus ,, clockwise turning
⧗ ,, ,, counter-clockwise turning
The steepness is different for sensation (8 sec) and nystagmus (16 sec).
The threshold for sensation is 2.5°/sec impulse and 5°/sec for nystagmus; the latter is usually higher.
(GROEN, *J. Laryngol.* 67, 894, 1957).

to him during the braking time, this giving rise to a turning sensation and nystagmus. Owing to its inertia the endolymph makes the cupula bulge out, after which the cupula very slowly returns to its position of equilibrium. During this period the subject experiences the sensation of turning with constantly decreasing angular velocity. The nystagmus also decreases. The durations of the sensation and of the nystagmus are usually taken as a function of the angular velocity just before braking. The reaction times are plotted against the logarithm of the angular velocity which gave rise to them. The 'normal' cupulogram (Fig. 10, VAN EGMOND, JONGKEES and GROEN) shows two straight lines, which, remarkably enough, make an angle with each other. The slope of the normal sensation line is about 8 seconds, that of the nystagmus normally 12 seconds.

Central inhibition

At first sight it seems strange that the decay of the cupula, which forms the basis of the two curves, should be represented by different slopes.

This is a discrepancy (GROEN, 1956) which, as evidenced by all kinds of experiments on the peripheral organ, can only be accounted for by a difference in stimulating action in the central nervous system. There is a certain group of subjects who do not show this discrepancy: their sensation and nystagmus curves run parallel with a slope of 20 seconds or more.

Although otherwise perfectly healthy, all these subjects have one characteristic in common: they are very sensitive to motion sickness; these people evidently possess normal organs of equilibrium, but the central elaboration of the stimulus takes place without the inhibiting action of the central nervous system. The communications of the vestibular system with other systems are also not inhibited, so that, for example, the autonomic nervous system undergoes a much stronger influence than would be the case in normal persons under identical conditions of stimulation.

In these abnormally steep cupulograms of sufferers from motion sickness the uninhibited elaboration of the rotatory stimuli is thus demonstrated. DE WIT has shown that an increased reaction to linear stimuli is associated with an increased reaction to rotatory stimuli. The parallelism between the central elaboration of stimuli

originating from crista and macula was demonstrated by submitting the same subject to a series of oscillations on a parallel swing, in which the gradient of the retinal blood pressure was measured as indicator of the autonomic sequelae of the stimulus, and to a cupulometric examination.

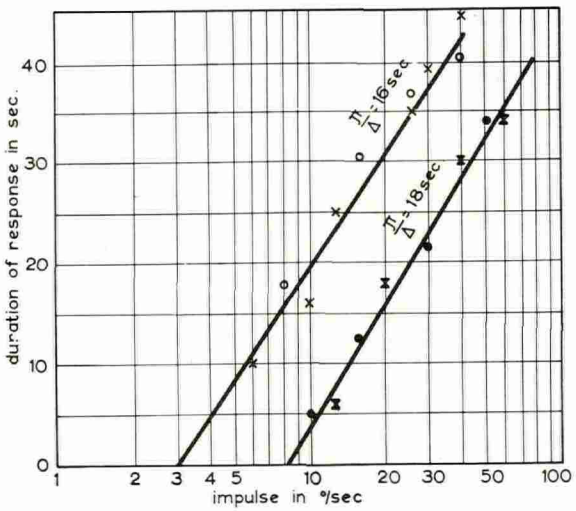


Fig. 11.

Case of hypersensitivity to motion sickness. Parallelism between sensation (16 sec) and nystagmus (18 sec). The thresholds are normal.

As cupulometric examination is a simple and accurate procedure, it has been used without a supplementary otolith examination in various investigations on this problem of central elaboration (De Wit).

A normal person thus possesses the ability to regulate centrally the influence on other areas of activity starting from the vestibular nuclei. Sensation, as the ultimate projection on the cerebral cortex of what happens in the organs, is the most subject to this central regulation. Nystagmus, which rather behaves like a reflex mechanism, is less influenced, although here also the inhibition is demonstrable.

It also appears that a normal person is able to increase this

inhibition, so that the sensation and nystagmus cupulograms become still flatter. This not infrequently occurs in persons who have to live under conditions that are abnormal for the vestibular system. e.g. fighter pilots (KRIJGER). The cupulograms of these pilots become normal again after a few weeks' leave.

The tendency to inhibition is evidently a result of the conditions.

Central pathways of the vestibular system

The vestibular nerve forms together with the cochlear nerve the acoustic nerve. Phylogenetically, the vestibular nerve is the older.

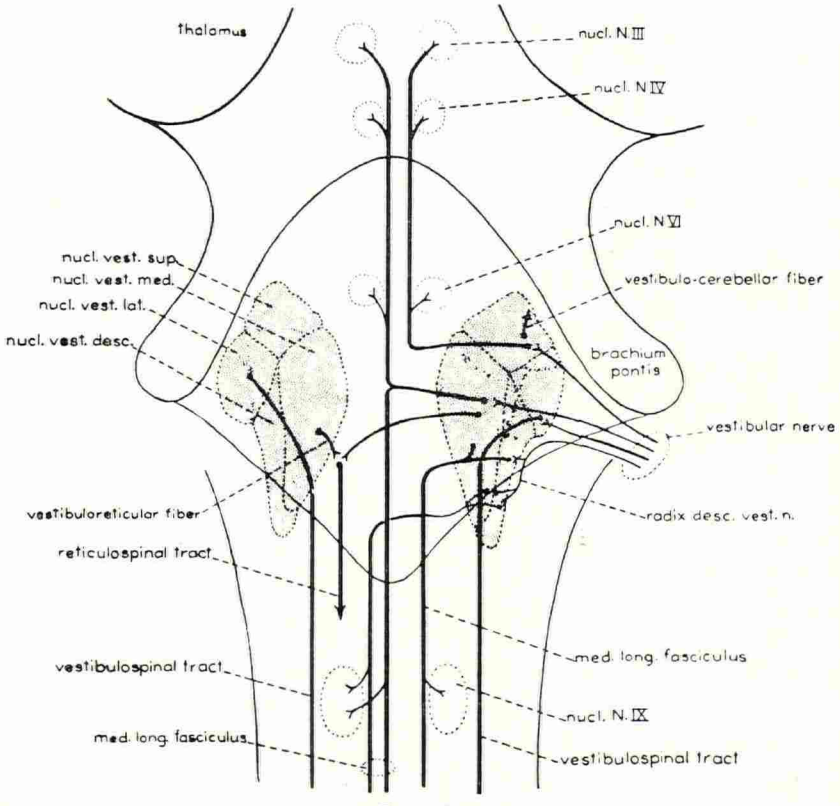


Fig. 12.

Vestibular nuclei and pathways in the brainstem.
(SPIEGEL and SOMMER).

In all vertebrates, stimulation of the sensory cells of the cristae ampullares and of the maculae acusticae produces reflexes which regulate the position and the movements of the body. In the lower Vertebrates (fishes) an alarm reaction is produced by the rhythmic stimulation of the maculae sacculi by sound vibrations (up to about 1400 cps); in other words, we can already speak of an auditory function. However, the first animals in which a separate organ of hearing begins to develop in the labyrinth are the amphibians: in addition to the nerve for the organ of equilibrium a separate nerve for the organ of hearing develops. In view of this development, it is understandable that the two nerves as they emerge from the petrous bone are united in one bundle, that there are communications between them in the peripheral organ, and that their pathways coincide partially in the central nervous system.

Only the vestibular nerve need be considered in connection with the pathogenesis of seasickness, which is mainly due to a specific way of stimulation of the otoliths. We shall therefore refrain from further discussion of the course of the cochlear nerve with its pathways in the central nervous system, and shall only give a brief description of the course of the vestibular nerve and its communications.

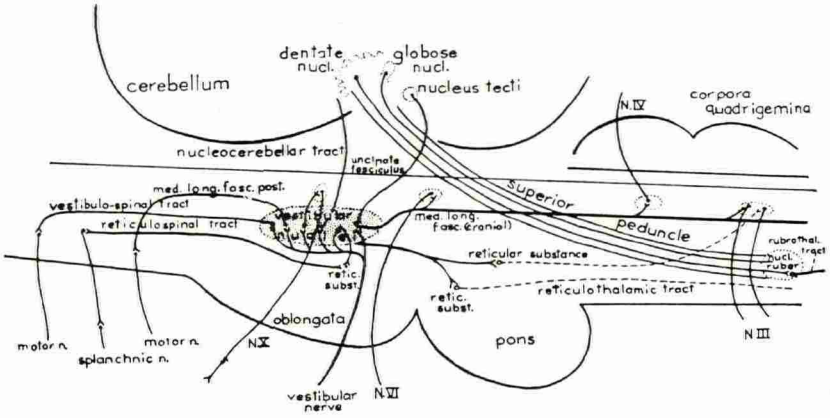


Fig. 13.

Vestibular nuclei and pathways in the brainstem.
(SPIEGEL and SOMMER).

For a better understanding of this we refer to the two diagrams, reproduced from BAST and ANSON, and SPIEGEL and SOMMER (Figs. 12 and 13), in which special attention is given to the connection with the reticular substance.

The vestibular nerve originates in the bipolar cells of the ganglion of SCARPA, which is subdivided into two parts, the ganglion superius and the ganglion inferius or ganglion sacculi. The peripheral extensions from the ganglion superius run to the macula utriculi and to the crista of the horizontal and of the anterior vertical canal, while the extensions from the ganglion inferius run to the macula sacculi and to the crista of the posterior vertical canal.

The central offshoots of the ganglion sacculi run for the main part to the nucleus ventralis of the cochlear nerve. The central communications of these fibres go, together with the central connections of the cochlear nerve, to the lateral lemniscus, but are interrupted in various nuclei (nucleus corporis trapezoides, nuclei lemnisci laterales). The latter nuclei send fibres to the fasciculus longitudinalis medialis and thence to the motor nuclei. The central extensions of the ganglion superius plus a small part of the fibres from the ganglion inferius (sacculi) run to the vestibular nuclei in the medulla oblongata, viz.: to the nucleus superior (BECHTEREW), nucleus lateralis (DEITERS), nucleus medialis or triangularis (SCHWALBE) and nucleus inferior (spinalis).

There are also some fibres which pass, without interruption, as a narrow bundle through the corpus restiforme to the nuclei of the cerebellum, and partially to the flocculus (tractus vestibulo-floccularis). From the nucleus of BECHTEREW ascending fibres proceed to the fasciculus longitudinalis medialis of the homolateral side and thus to the nuclei of the ocular muscles. From the nucleus of DEITERS, stimuli from the peripheral vestibular organ are transmitted to motor cells of cranial and spinal nerves via the tractus vestibulo-mesencephalicus and the tractus vestibulo-spinalis. This nucleus (DEITERS) also gives off fibres to the cerebellar nuclei. From the nucleus of SCHWALBE ascending fibres run to the fasciculus longitudinalis medialis of the crossed side and thus to the nuclei of the ocular muscles.

From the nucleus inferior, descending fibres course to the fasciculus longitudinalis medialis of the crossed side to the anterior horn

cells of the whole spinal cord. Fibres from the cerebellar nuclei run as fasciculus cerebello-rubro-thalamicus to the nucleus ruber. Here the tractus rubro-spinalis begins, which gives rise to crossed fibres running to the anterior horn cells of the spinal marrow.

The reflexes which are caused by the flow of stimuli from the peripheral vestibular organ to the central nervous system, and thence to the motor nuclei of the muscles of head, trunk and extremities (and on which a moderating influence is exerted by the connection with the cerebellum) take place unconsciously on normal displacements and movements of the body.

Only abnormal stimuli, as, for example, in vestibular examinations, give rise to abnormal reactions in walking, grasping, etc., and these produce uncertain and usually disagreeable sensations. There must also be communications from the peripheral vestibular organ to the vaso-vegetative system; under normal conditions these communications exert a regulating influence on blood vessels, intestinal movements, respiration, pupils etc. On normal stimulation, nothing of this is observed, but on excessive stimulation they give rise to all sorts of manifestations like those occurring in seasickness. Less is known about the direct communications of the organ of equilibrium with the centres of the sympathetic and parasympathetic systems than about the motor reflex pathways. That these exist is shown by the fact that labyrinthectomized human beings or animals never become seasick. The cerebellum is the most important centre for the regulation of these reflexes. This has been demonstrated by BARD and coworkers, who were no longer able to provoke seasickness in dogs after removal of the cerebellum. It seems that fibres coming from the nucleus triangularis (SCHWALBE) are in direct communication with the autonomic centres in the medulla oblongata. DEL BO and LIVAN have demonstrated the existence of autonomic fibres which spread in the network of motor nerve fibres under the macula utriculi, where they are no longer visible individually; the fibres are in communication with the stellate ganglion.

Further, all the vestibular nuclei are connected with the reticular substance. This system, which is present throughout the length of the spinal cord, between anterior horn and posterior horn, and in the medulla oblongata, borders in its upper part on the hypothalamus, the centre of all autonomic activity. As there is clear evidence

of coupling between the vestibular and autonomic systems, this coupling must presumably run from the reticular substance to the hypothalamus (see Fig. 14).

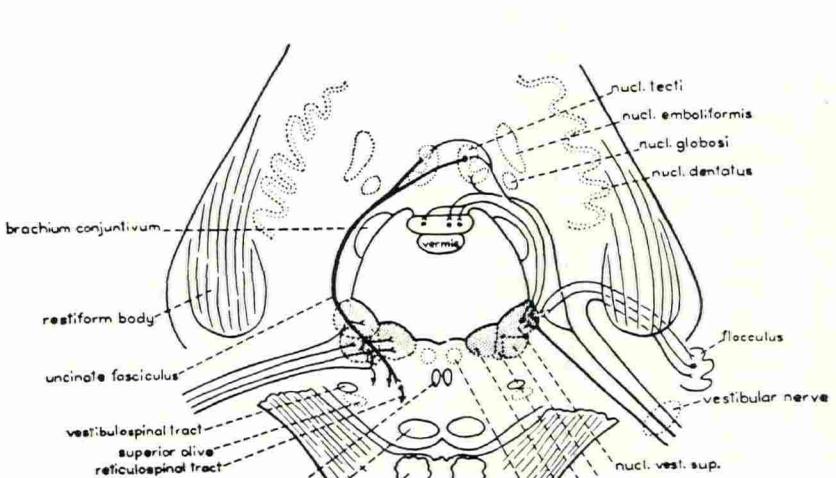


Fig. 14.

Diagrammatic representation of the vestibular pathways to the cerebellum. In addition to the second order neurons from the vestibular nuclei, a primary neuron is indicated here as terminating in the cerebellum.
(BAST, T. H. and ANSON, B. J.: *The Temporal Bone and the Ear*, Springfield, Ill., CHARLES C. THOMAS, p. 100, 1949).

Cerebral connections

Impulses originating in the labyrinth also reach the cerebral cortex, as stimulation of the labyrinth causes the conscious sensation of giddiness. We do not yet know the pathways along which these impulses are transmitted. Experiments carried out by SPIEGEL on dogs and cats (in 1932 and 1934 respectively) showed that an area of the temporal lobe receives the stimuli from the vestibular apparatus. PENFIELD and CAGE (1933) also believe that stimulation of the posterior part of the temporal lobe in human beings sometimes gives rise to a sensation of dizziness. KEMPINSKY (1951) stimulated electrically — with bipolar electrodes — the vestibular part of the

VIIIth nerve, and studied the manifestations which then arose in the cerebral cortex.

His conclusions are as follows:

1. the cortical receiving area of the vestibular portion of the VIIIth nerve has been outlined by single shock stimulation of the 'isolated' vestibular nerve in the cat.
2. The centre of this vestibular sensory area lies in the anterior descending limb of the suprasylvian gyrus. Anteriorly it overlaps the posterior margin of the arm and face tactile receiving areas, and posteriorly it appears to overlap the anterior margin of the auditory receiving area.
3. The ipsilateral and contralateral cortical projections are symmetrical in extent and location.
4. No cortical projection of possible efferent fibres of the facial nerve could be demonstrated, although one cannot exclude a projection from the nervus intermedius to this cortical region.

These experiments lead to the assumption of the existence of an independent projection of the organs of equilibrium on the cerebral cortex. The existence of rotatory sensations and other sensations of equilibrium can therefore be explained from a direct 4-neuron connection between peripheral organ and cortex.

Transmission of stimuli as point of action for anti-seasickness drugs

There exists a hypothesis that some anti-seasickness drugs exert a direct action on the cholinergic system of the transmission of stimuli. DIAMANT (1954) considers it probable that in the vestibular nuclei this transmission is of the cholinergic type. The transmission of stimuli can be explained in the following way. The free acetylcholine causes a fall of membrane resistance to the transport of ions. First, however, acetylcholine must be liberated by the specific action of the nervous impulse (by K^+-ions) from the storage protein, to which it was bound; as soon as the acetylcholine has done its work it is hydrolysed to choline and acetic acid by cholinesterase. Then acetylcholine is formed again under the influence of the enzyme choline-acetylase in the presence of coenzyme A, adenosine triphosphate (ATP), Mg^{++}- and K^+-ions and storage protein, and stored temporarily. All drugs which

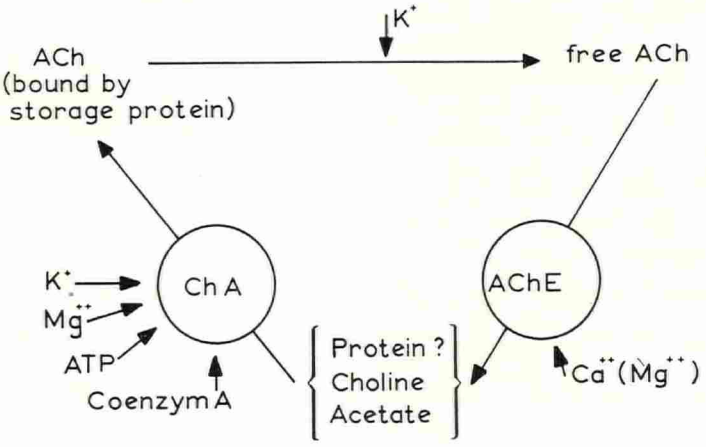


Fig. 15.

Acetylcholine cycle.
ACh Acetylcholine.
AChE Acetylcholinesterase.
ChA Cholinacetylase.
(SUMMER and MYRBÄCK. *The Enzymes* Vol. I, Part I, page 443. Academic Press Inc. New York 1950).

counteract the production of acetylcholine or enhance the action of cholinesterase, would therefore be expected to exert an inhibiting effect on the transmission of stimuli. Thus they would weaken the coupling between the vestibular and the autonomic system, and in this respect they might work as anti-seasickness drugs.

A good example of such a drug is the well-known anti-seasickness agent atropine, which is presumed to promote the esterase activity by which the transmission of stimuli is reduced. The drug diphenhydramine (known under various trade-names, among which Allergan, Benadryl, Benodine, Dimedrol), which has a corresponding action, is another good preventive of seasickness.

CHAPTER IV

SYMPTOMATOLOGY OF SEASICKNESS

DE WIT (1957) gives the following definition of motion-sickness, which therefore holds also for seasickness:

> 'By motion-sickness we understand the neurovegetative manifestations of a disagreeable nature which arise in persons sensitive to this disease when they are exposed to continuous and preferably irregular changes of speed'.

It is perhaps better to speak of 'disorder' than of 'disease', because all aspects of seasickness point to a dysregulation of the various functions, which are mainly of neurovegetative nature.

These neurovegetative manifestations are both sympathetic and parasympathetic in nature. In 1933 ROMEZ-GUILLIEZ declared that there are two clearly distinguishable stages in the course of every case of seasickness.

The first stage is dominated by the stimulation of the sympathetic system. This sympathicotonic stage (I) may be of very short duration, so that it is often not noticed. That this first stage indeed exists has been demonstrated in the laboratory by means of the parallel swing, on which the retinal blood pressure rises in persons sensitive to seasickness after they have been subjected to stimulation of the otolith organs for one minute (HULK and HENKES).

In the second stage it is rather the manifestations of parasympathetic stimulation which come to the fore. We can therefore speak here of the parasympathicotonic stage (II).

Every case of motion-sickness, i.e. also of seasickness, begins with:

I. Sympathicotonic stage

a. headache, of migraine-like character, and caused by a rise of intracranial blood pressure;
b. mild tachycardia;
c. pallor of the face.

On continued and/or stronger stimulation the signs and symptoms caused by the predominance of the parasympathetic system appear, culminating in the 'nausea syndrome'.

II. Parasympathicotonic stage

a. general malaise;
b. bradycardia. The original tachycardia is replaced by a slowing of the pulse, due to predominance of the parasympathetic influence;
c. a fall of blood pressure, caused by relaxation of the vasoconstrictors and the coming into action of the vasodilators;
d. cold sweat;
e. pollakisuria;
f. increase of intestinal peristalsis which, with the increased intestinal fluid secretion leads to diarrhoea;
g. hypersalivation; this may become so severe that patients whose self-control is poor may even begin to dribble;
h. vomiting, which may become so violent that even bile is brought up, not infrequently mixed with blood due to traumatization of the gastric wall.

These sympathicotonic and parasympathicotonic actions are regulated by the hypothalamus, which, in this respect, receives its commands from the reticular substance. Regarded from the viewpoint of the 'alarm' action of the reticular substance, we have here the picture of a system dysregulated by excessive 'alarms' (STARZL, TAYLOR and MAGOUN). Hence 'disorder' is a better term than 'disease'.

In seasickness this excessive alarm effect is produced mainly by aspecific stimuli from the sense organs. Seasickness can therefore be regarded as an overstimulation syndrome starting from vestibular impulses. The same effect can be produced by stimuli from other sense organs, such as acoustic, visual, olfactory and pain stimuli and stimuli from the proprioceptive system or from the cerebral cortex (psyche). In this case we may get a summation of stimuli.

This may explain why a person more easily becomes seasick in a stuffy, confined space. Under these conditions the olfactory stimuli also begin to exert an influence. A seasick person prefers to lie flat on his back in his bunk, for in this position the stimuli from the proprioceptive system are almost completely eliminated.

CHAPTER V

EXPERIMENTAL INVESTIGATION

This investigation was carried out during a voyage from Rotterdam to New York and back on board the ss 'Maasdam', in an attempt to gain some understanding of the relationship existing between certain physical stimuli and the reactions to these stimuli, which eventually lead to seasickness.

The changes in acceleration must be regarded as the most important stimuli, especially the changes of vertical linear acceleration.

To measure these accelerations and to record them we used selfrecording accelerometers.

There are various systems of measuring accelerations. For our investigation the most suitable method was the use of directly-recording mechanical instruments, for which no gyroscopes, complicated electronic auxiliary apparatus or long electric wiring are required; this also gave the advantage of easy displaceability. The accuracy of these mechanical accelerometers was more than sufficient for this investigation.

In a previous chapter it was shown that the otolith organs can be regarded as the receptors of the linear accelerations applied. These impulses are further worked up in the vestibular system and result in certain reactions.

In the laboratory these reactions can be studied by observers or recorded by means of complicated instruments such as, for example, the turning chamber, the torsion chamber, the torsion swing, or the parallel swing.

On board ship, however, it is impossible to test every passenger or member of the crew individually. We had to draw our information from the statements of their own experiences given to us by each

person. To record these we used a questionnaire form, which was given to every passenger and member of the crew; this was done with the help of the ship's administration. One day before it was made known to everybody, by posters, that this investigation was to take place, and its reason and purpose were explained as clearly as possible. In this way we hoped that everybody would be willing to cooperate, and we were not disappointed in this hope. Captain, officers, crew and passengers all gave us their full cooperation, without which such an investigation would have had little chance of success.

The cabin stewards supplied us every day with an exact statement of the number of seasick persons. GROEN and I held daily sessions of some hours' duration to take in the completed questionnaire forms.

This gave us at the same time the opportunity to assist the passengers and crew in filling in their forms. This was necessary, for experience taught us that many persons, especially when seasick, needed some help.

In this way we succeeded in getting back a high percentage of the forms correctly filled in; thus we obtained possession of many valuable data which later, in the Utrecht laboratory, were classified and statistically analysed.

The curves of the accelerometers were accurately analysed in the laboratory, tabulated and then, according to a certain standard equation, reconverted into acceleration values.

We were able to draw some interesting conclusions from the data obtained in this way, as will be shown in the following pages.

CHAPTER VI

METHOD OF MEASUREMENT

In this chapter, dealing with the measuring technique, the whole instrumentarium will be described, as regards both the source of the stimuli and the recording aparatus. As in our case the stimuli were caused by the movements of the ship, these must first be discussed.

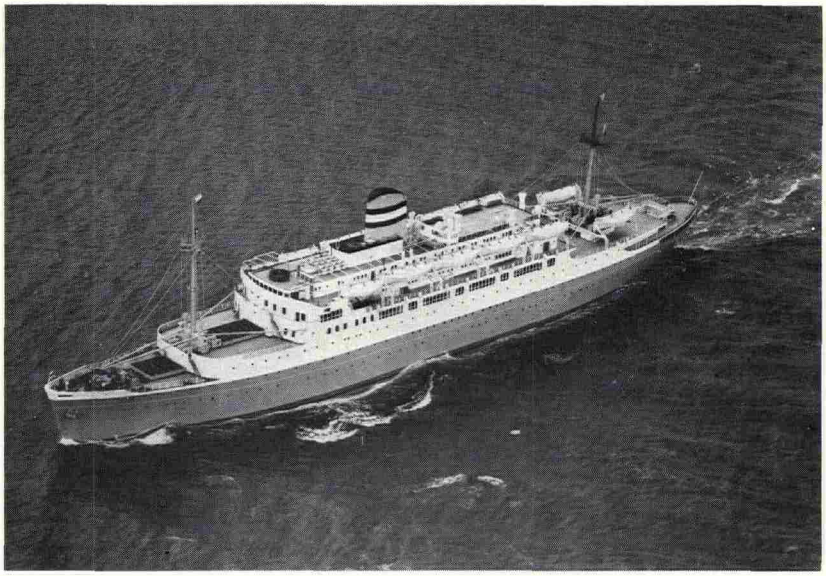
A large proportion of the measurements were taken on board the 'Maasdam'. The dimensions of this ship are length 149 metres, beam 21 metres and draught about 8 metres, with a tonnage of 15,015 tons gross. The maximum number of passengers she can carry is about 1100.

A questionnaire form was drawn up (Fig. 17) and handed out to the passengers after they had been on board for two days. In the meantime, the ship's movements in the three main directions were recorded by means of automatic linear accelerometers so that, by comparison of the curves obtained with these meters and the questionnaire material received back, the relationship between stimulus and reaction could be studied.

The ship's movement as physical stimulus

The persons aboard a ship must necessarily take part in the ship's movement. What is this movement exactly? It can be described as a collection of translations and rotations with respect to an axial system of the ship. The longitudinal axis of the ship will be called the X-axis, the transverse axis the Y-axis, and the vertical axis the Z-axis. These movements are named as follows:

Translations in	X-direction	surging
,,	,, Y-direction	swaying
,,	,, Z-direction	heaving



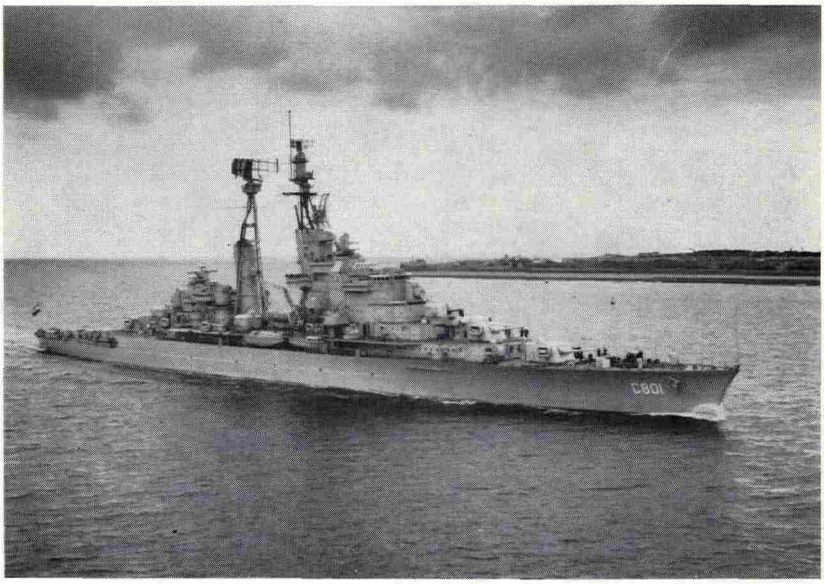


Fig. 16.

s.s. 'Maasdam', of the Holland-America Line,
and H.M. 'De Ruyter', a cruiser of the Royal Dutch Navy.

Rotations about X-axis		rolling
,,	,, Y-axis	pitching
,,	,, Z-axis	yawing

The movement of a ship at sea will consist of a composition of the six movements mentioned, so that the whole can become very complicated. When a well-constructed and well-trimmed vessel sails

Holland-America Line s.s. MAASDAM STATE UNIVERSITY OF UTRECHT DEPARTMENT OF OTOLARYNGOLOGY

The following questionary is part of a scientific research on seasickness. It is arranged by the State University of Utrecht (Holland) in kind co-operation, with the Managing-Directors of the Holland-America Line and performed by Mr. J. H. Nieuwenhuijsen M. D. and Mr. J. J. Groen Ph. D.

We kindly request your voluntary co-operation to provide us with the necessary information, which data will be gratefully accepted by us.

QUESTIONARY

1. Age	5-3 Yrs
2. Sex	Female
3. Have you ever been at sea before?	no
4. Were you seasick then?	—
5. Was the sea rough, normal or calm?	Calm
6. Are you seasick soon?	next day after starting
7. What are your sensations?	extreme nausea
a. nausea	yes
b. vomiting	yes
c. disorientation	yes
d. other phenomena.	
8. Are you sensitive to other types of motion-sickness?	no
e.g. car-sickness?	no
9. Did you ever have a concussion of the brain or simular lesion and when did you have it?	no
10. Are you liable to having dizziness or vomiting even when not on board a ship?	no
11. Have you ever suffered from other diseases?	no

CONCERNING THIS TRIP:

12. At what time did you feel seasick. Please, give date and hour. If gradually, give date and hour approximately.	Nov. 1st about 8:30 am. Suddenly
13. Did you take any drugs against seasickness? What drug did you take and with what result?	Yes — 1 tablet. No result Could not retain it on stomach. Took 1 tablet
14. When did you take the drug? Already at the beginning of the trip or during it? Please, give date and hour of administration of the drug. Before or after meal?	before sailing — no more. 1st tablet 11:30 Oct 31, before sailing. (30 mins. before Sailing) Before
15. If you want to add any remarks to this questionary, you are invited kindly to do so here or overleaf.	No extreme dizziness experienced — Only Nausea for about 2½ days

Fig. 17.

Questionary handed out to the passengers aboard the 'Maasdam'.

over a normal sea, the most important movements remaining are: pitching and rolling.

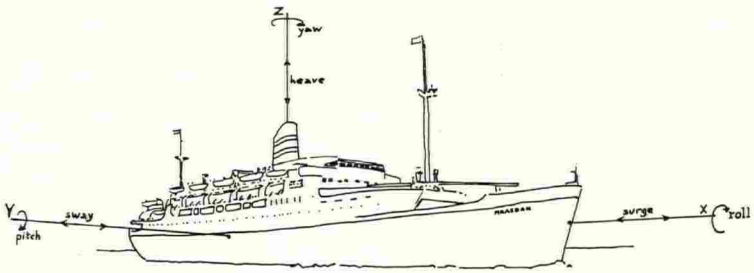


Fig. 18.

The cartesian axis system and the terms of the translations and rotations in relation to this system.

The properties of these movements are determined on the one hand by the sea and on the other hand by the ship and its course. When a ship is stopped on a smooth sea and brought out of its equilibrium position (about the X-axis) by an external force, and then left free, it will begin to roll. The captain can to a certain extent control the period of this movement by distributing the contents of the oil and water tanks over the ship in a certain way by means of an intricate system of pipes and pumps. Usually the rolling period (properly speaking, the vibration period), which is the time needed for a complete pendular movement from port to starboard and back, is made as long as possible, that is as far as the stability and therefore the safety of the ship permit. A long rolling time involves the chance of a large angle of roll, which is again not favourable for the passengers' comfort. However, practice has shown that slow rolling causes the least seasickness. The rolling period chosen by the captain is therefore a compromise between safety and comfort. In the case of the 'Maasdam' it was 18—21 seconds. When the theoretical disturbance of equilibrium does not act transversely in the Y-direction, but perpendicularly to the bow (parallel to the Z-axis), the ship will begin to pitch when left to itself. The captain can do little to influence this period. When the ship carries a normal cargo, the pitching period is further determined by the form of the ship. The pitching period can be varied only very slightly by stowing the

cargo in a somewhat different way; for the 'Maasdam' it was about 7 seconds. As the movement is only sinusoidal for small angles, the pitching period is not constant when the angles increase more and more; on account of the form of the ship, the directional forces increase less than proportionally, so that the movement slows down when the pitching increases. The ship's movement is therefore not characterized by a constant pitching angle; on the contrary, the pitching repeatedly waxes and wanes, starting from zero, reaching a maximum after, for instance, three or four pitching periods and then dying down again to practically zero, after which the ship again begins to pitch (see Fig. 19). There is a constant interaction between the wave trains of the sea and the resultant movement of the ship. The whole has the form of a forced vibration, which repeatedly gets out of phase, to be forced back into it subsequently.

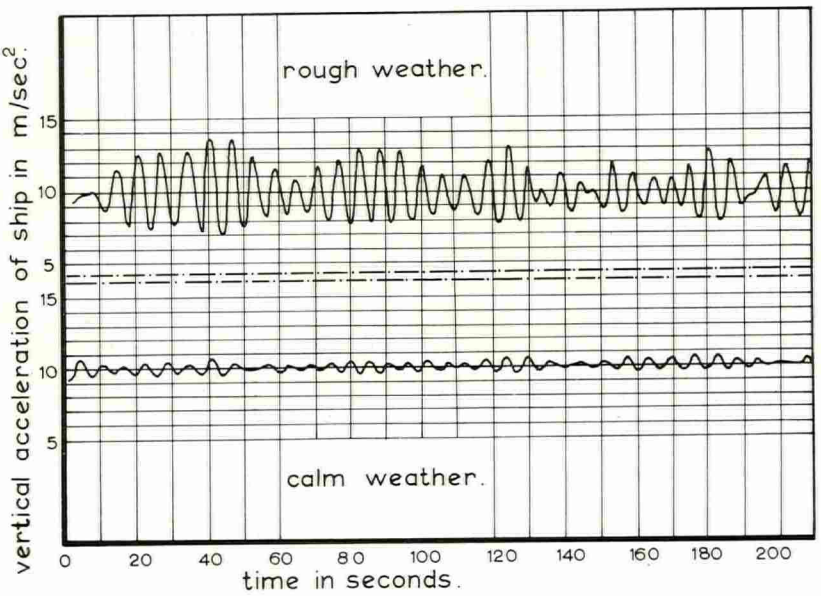


Fig. 19.

Pitching of ship under the conditions of rough and calm weather, expressed in m/sec² vertical acceleration in the average situation on the ship. Pitching period 7 seconds.

During the voyage the average passenger was subjected to an average vertical amplitude of about 1 metre, which means a movement up and down over a distance of 2 metres. The vertical linear acceleration to which the test persons were subjected was thus on an average $g \pm 1$ m/sec^2. In heavy weather this became $g \pm 2.5$ m/sec^2, in which case the passenger made vertical movements over a distance of about 5 metres. On the other hand, even with the greatest rolling angles (15°), the vertical acceleration of the average passenger was only about 0.15 m/sec^2, which is a negligible factor compared with the effect of pitching.

Measuring apparatus

To measure the accelerations we had three different accelerometers at our disposal, namely GROEN's 3-D accelerometer, the MASPI accelerometer and an angular accelerometer of our own design.

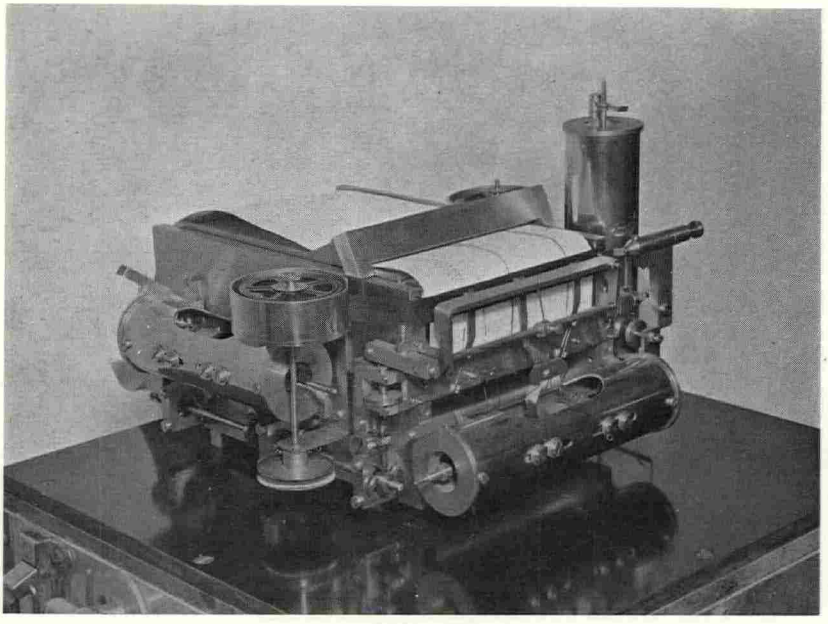


Fig. 20.

Automatically recording 3-D linear accelerometer. The positions of the three needles are recorded four times per second by means of a hammer mechanism via a typewriter ribbon.

a. GROEN's *3-D accelerometer*

This acceleration meter was designed by GROEN in the laboratory for labyrinthology of the Otorhinolaryngological Clinic of the University of Utrecht, and constructed by chief instrumentmaker VAN KLAVEREN. This instrument records linear accelerations in three

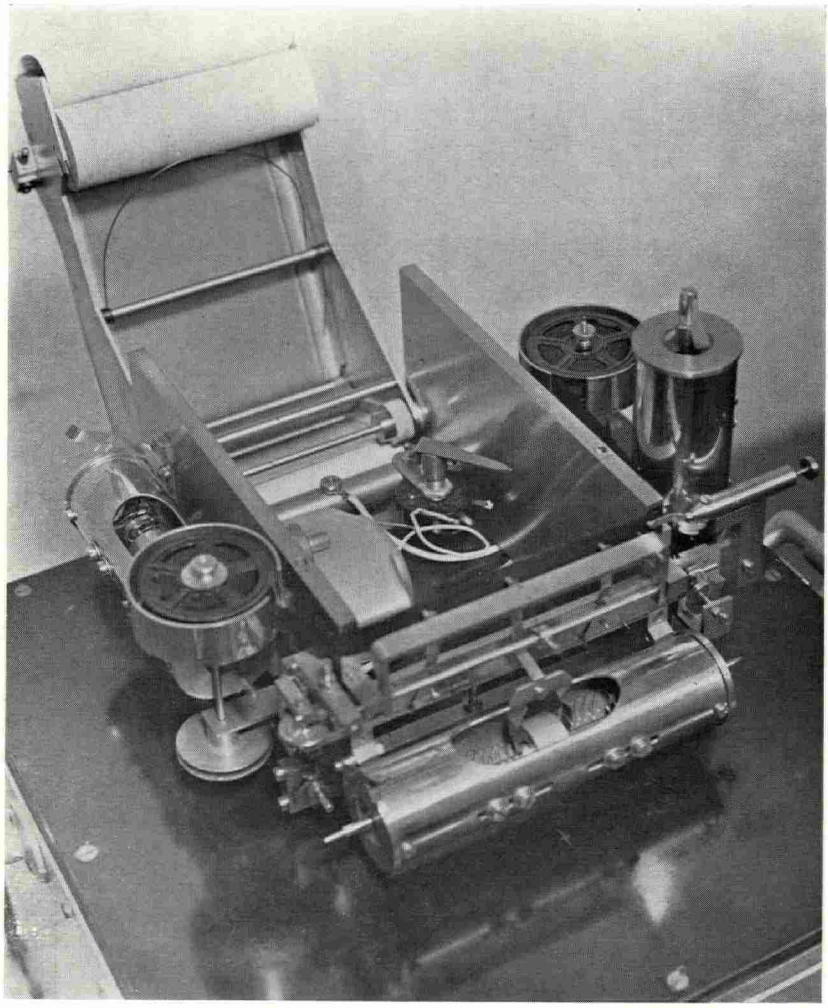


Fig. 21.

As in Fig. 20. Instrument opened.

mutually perpendicular directions (Fig. 21). Each of the three directions has its own accelerometer, which consists of a brass weight of 200 g fixed to a hard steel pin, which is supported on both sides by a system of three rollers placed at angles of 120° to each other. The friction is kept as low as possible by means of these roller-bearings. The brass weight is kept in place by two spiral springs. By suitable selection of the stiffness of these springs it was found possible to adapt the accelerometer to the particular purpose of measuring the accelerations which occur aboard ship under all sorts of conditions. The sensitivity for 1 g acceleration was as follows:

α. in a longitudinal direction 35 mm deflection of the pointer,

β. in a transverse direction 50 mm deflection,

γ. in a vertical direction 38 mm deflection.

The indication time was about 0.35 seconds for the longitudinal and vertical directions, while for the transverse direction it was about 0.45 seconds.

Compared with the ship's movements, in which in our case no periods shorter than 4 seconds occurred, these indication times are negligibly short, so that the accelerometers really record quantitatively the momentary values of the acceleration. A fine steel wire is attached to each pin; this wire is connected to a writing point. The three writers are joined up on a sliding system of two very taut steel wires. The connection between the weights and the writing points is kept taut by a number of springs. Behind the writers themselves a heavy ruler is fixed; this is made to impinge four times per second against the writers from behind, by means of a special device. A typewriter ribbon is passed between recording paper and writers; in this way the paper, which is 12 cm wide, receives four times per second an impression of the positions of the three writing points; the paper moves with a speed of 1 mm per second. Each of the three records therefore consists of a dotted line, which also provides a measurement of time. The stroke mechanism regularly blocks the movement of the accelerometer for a short time, so that sufficient damping results. A fourth writer can if required be put into action at the edge of the paper to indicate particular moments of time. Paper, hammer and ribbon are moved by a 12 volt DC motor, fed by an accumulator. The same instrument was used in experiments on ships' movements by the Royal Dutch Navy, in which the effects

on the persons on board were also studied by means of a questionnaire (see Chapter VII).

b. The MASPI *accelerometer*

The second linear accelerometer used was an existing French instrument (trade-mark MASPI), which was modified by us to make it suitable for the measurements of accelerations on board ship. This apparatus records the linear accelerations in one particular direction.

The MASPI accelerometer consists of a tube-shaped steel container filled with mercury, which acts as a mobile heavy mass. The mercury column is bounded on both sides by a rubber membrane; adjoining one of the membranes is a chamber filled with air, the pressure of which can be regulated. This air cushion works as an adjustable elastic system. Adjoining the other membrane is a chamber filled with glycerol, which is in communication, via an adjustable cock, with a BOURDON manometer. This cock serves to regulate the damping. The manometer is connected to a pointer moving over the recording paper, which is slowly moved on by clockwork. The sensitivity for g is 25 mm. deflection. To mark the time, an electromagnetic writer is attached at the edge of the recording paper; this writer is connected to a chronograph which gives one impulse per second.

As we had two linear accelerometers at our disposal, we were able to take measurements simultaneously at two different sites on the ship. Synchronization was obtained by starting two stopwatches at exactly the same moment five minutes before the measurement. During the measurement, a time signal was given at intervals of one minute. During the five minutes elapsing between the starting of the stopwatches and the beginning of the measurement, one of the investigators had ample time to proceed to his post at the second accelerometer.

c. Accelerometer of our own design

The author had previously designed an angular accelerometer, which instrument was manufactured by KIPP & Sons, of Delft. The sensitive part of the apparatus consists of two weights, mounted diametrically opposite each other on a rod; normally the rod is in a vertical position and is kept in place by two steel knife-edges resting in agate bearings. The whole system is accurately balanced. A system

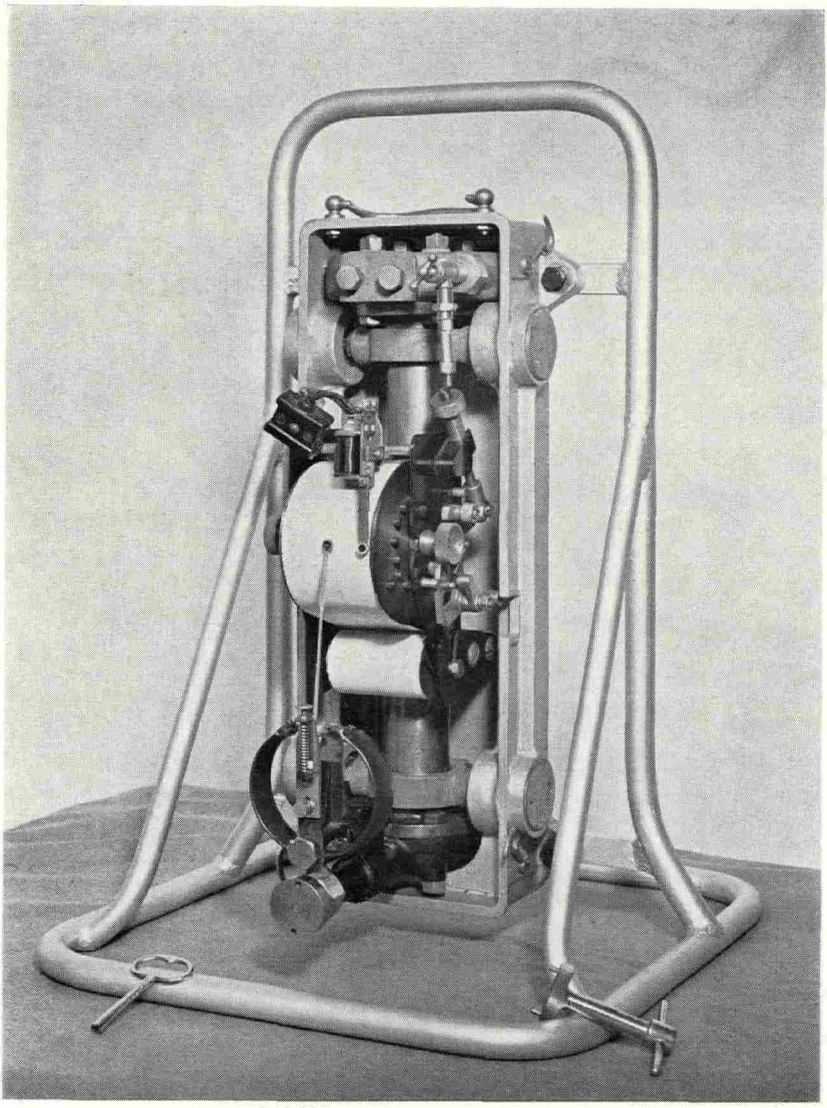


Fig. 22.

The MASPI linear accelerometer.

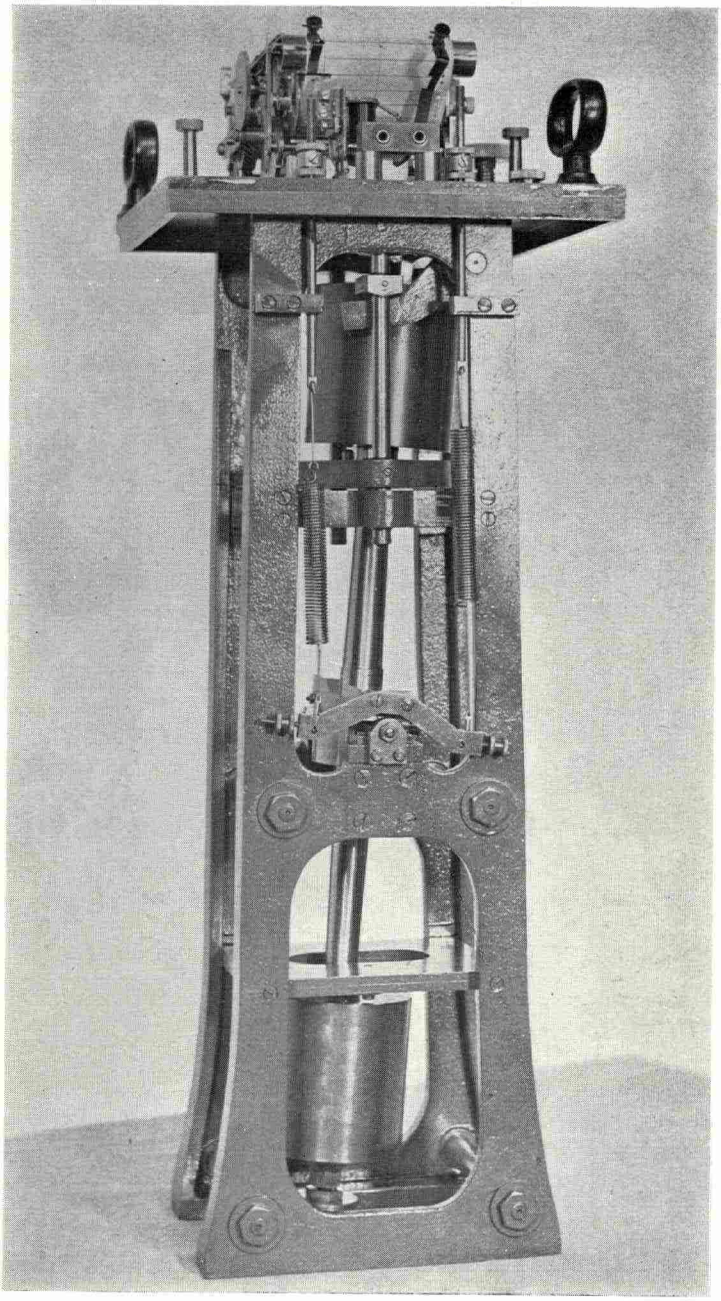


Fig. 23.

The angular accelerometer designed by the author.

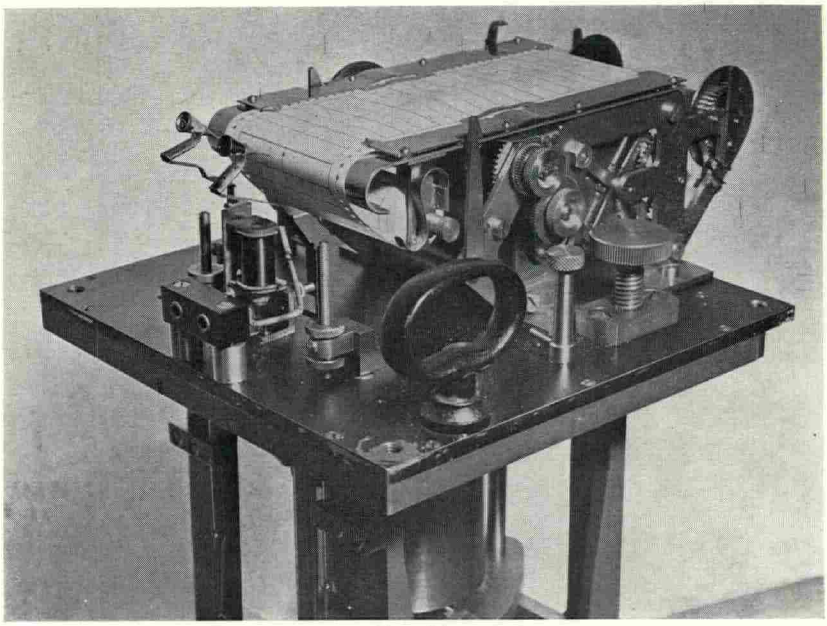


Fig. 24.

Detail of the recording mechanism of the accelerometer.

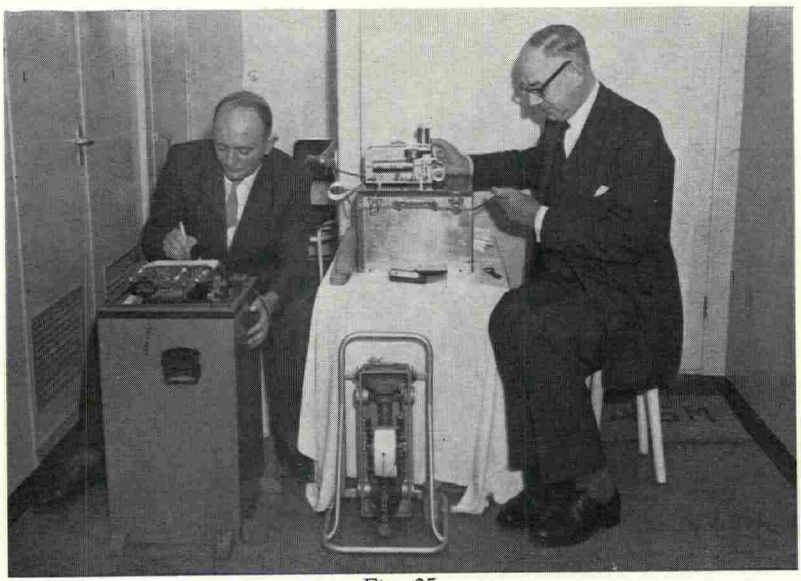


Fig. 25.

The three accelerometers together in action; checking of the performance.

of two adjustable springs ensures that the rod with the weights remains in the same position with respect to the casing. In this way a torsion swing is formed, with a natural period of 4.0 seconds. To damp this system the swing as a whole is immersed in a bath filled with oil of known viscosity. The movement is then practically critically damped with an indication time of 4.3 seconds. A pointer is attached to the rod, protruding far above the oil level and recording the deflections with an ink-writer on paper. This instrument was used to record the angular accelerations of the rolling movements.

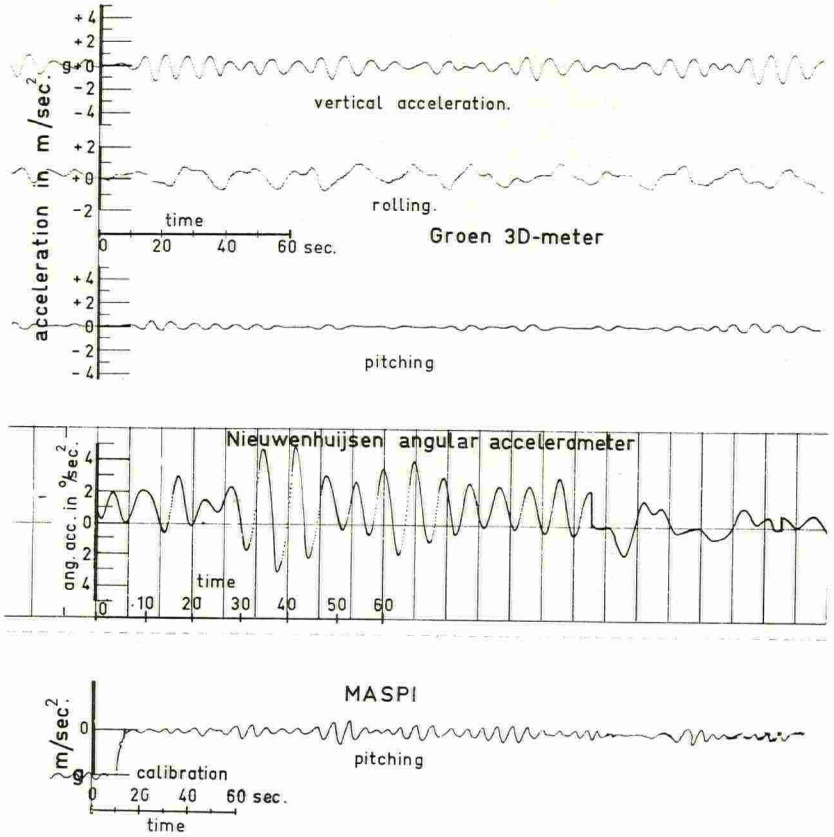


Fig. 26.

Typical recordings of the three accelerometers. The calibration of each is indicated in the ordinate; the abscissa shows the time. The recording by the angular accelerometer pertains in this drawing to the pitching of the ship.

The rolling period was 18 seconds, which is a long time compared with the natural period of 4.0 seconds; a correction of the curve was therefore necessary. The deflections are then 8 % too large.

The three instruments used by us were tested by GROEN in the above-mentioned labyrinthological laboratory.

It appears from the measurements with the angular accelerometer that on a normal sea the angular accelerations during rolling are of the order of magnitude of the minimum perceptibile of the system of semicircular canals. Even on a heavy sea the maximum angular acceleration does not become higher than $1.5°/sec^2$, and this only for a short time, so that the maximum angular speed which would then be active as a stimulus would become 4.5°/sec at most, which is only little above the threshold (2.5°sec).

QUIX and WERNDLY also arrived at the conclusion that the semicircular canals are practically not stimulated during a sea voyage.

This was once more checked with the help of this accelerometer; the correctness of QUIX's statement that it is not the semicircular canals but the otoliths which cause seasickness was thus demonstrated experimentally by the observation that the stimulation of the semicircular canals was only slight.

CHAPTER VII

RESULTS AND DISCUSSION

On the return voyage from New York to Rotterdam we were so fortunate as to be able to study the manifestations of seasickness in patients who had not yet become accustomed to the motion of the ship. After an initially calm voyage the ship got into the tail of the hurricane called 'Hazel'.

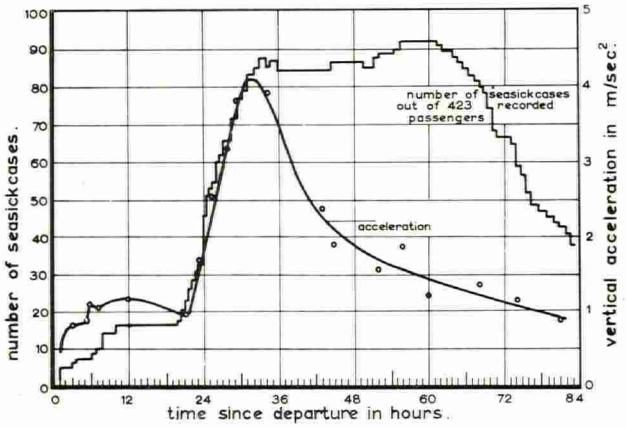


Fig. 27.

Seasickness as a function of time and variation in vertical acceleration. The continuous line represents the variation of the vertical acceleration in m/sec². (period 7 sec).

The broken line gives the number of seasick passengers as a function of time.

As the ship proceeded on its way, the movement of the sea increased rapidly, the maximum being reached after about twelve hours. The changes of acceleration had increased from 1 m/sec² to 4 m/sec² (see Fig. 27). In the beginning, when the average acceler-

ation was $g \pm 1$ m/sec^2, there were only 16 cases of seasickness (4 %) but this number had increased to 88, or about 22 % of the total of 423 passengers, when the ship's movements had reached their maximum. In the following hours the sea calmed down gradually. However, for the time being, the number of seasick persons remained almost constant and it did not begin to fall rapidly until after a day and a half from the onset of the more violent movement.

In the meantime the sea had settled down to a practically normal condition of $g \pm 1$ m/sec^2. The parallelism between the changes of acceleration and the number of cases of seasickness is very remarkable. It shows that only a short time elapses between the stimulus and the reaction following it. According to our questionnaire, this time was a quarter of an hour at most, the sensation of nausea being taken as a criterion. On the further voyage the movement of the sea was occasionally worse than ± 1 m/sec^2, but we no longer found any significant influence of this on the number of seasick persons.

In the other survey (see page 72), which concerned personnel of the Royal Dutch Navy, we were able on several occasions to study how much time elapsed between the appearance of the first symptoms and the culminating point of the manifest nausea. We were also able to ascertain when the first improvement of the condition occurred, and subsequently when all signs and symptoms of seasickness had disappeared. This was done on a day with moderate movement of the sea, without vertical variations greater than 0.25 g. The movement of the sea increased slowly, but calmed down again in the course of the day; the ship passed the Bay of Biscay. The first unpleasant sensations were reported at about 9.40 hours, the maximum being reached at 11.00 hours. This condition of manifest seasickness lasted for more than four hours, after which it improved, all signs and symptoms having disappeared after 6.00 hours.

In this study the seasickness was far less severe than that recorded in Fig. 27 (return voyage of the 'Maasdam'); this is the reason why more than an hour passed between the onset and the culmination of the manifestations.

The adaptation had evidently become complete. However, the average passenger needs two or three days to become adapted. The

percentage of seasick persons as a function of the ship's movement can be calculated from the graphs (outward and return voyages); this is plotted in the following figure.

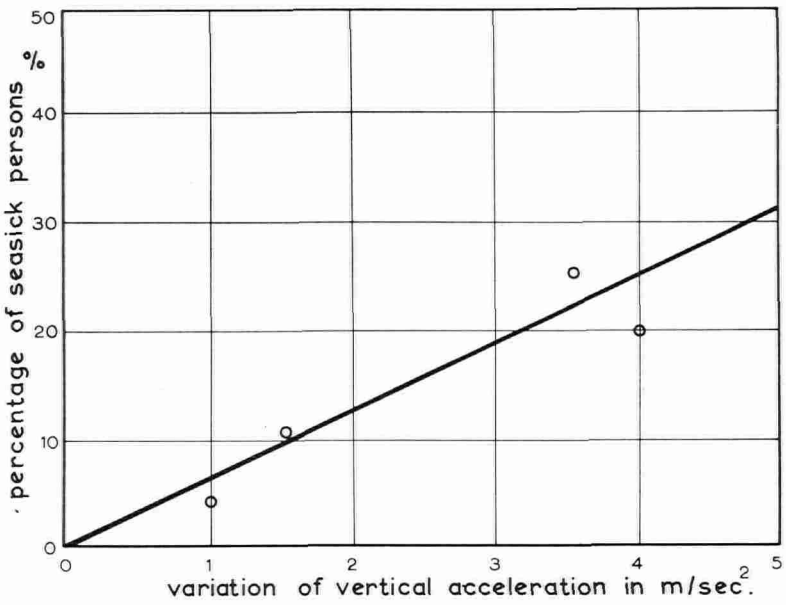


Fig. 28.

Percentage of seasick passengers as a function of the variation of the vertical acceleration. Pitching period 7 seconds.

To acquire an understanding of how people of various ages react to the movement of the sea, we made a distribution into age groups. We used groups of 0—10 years, 10—30 years, 30—60 years, and of 60 years and older; this distribution concerned both males and females. Another division was made between the passengers who used anti-seasickness drugs and those who did not take any special remedies. The curve given in Fig. 27, representing the number of seasick passengers, shows:

50 males who did not take anti-seasickness drugs; 13 of them became seasick.

30 males who did take these drugs; 22 of them became seasick.

30 females who did not use anti-seasickness drugs; 14 of them became seasick.

83 females who did take such drugs; 70 of them became seasick.

This is a total of 193 persons, 119 of whom became seasick.

These data are worked out as a function of age and plotted as a percentage in the following figure.

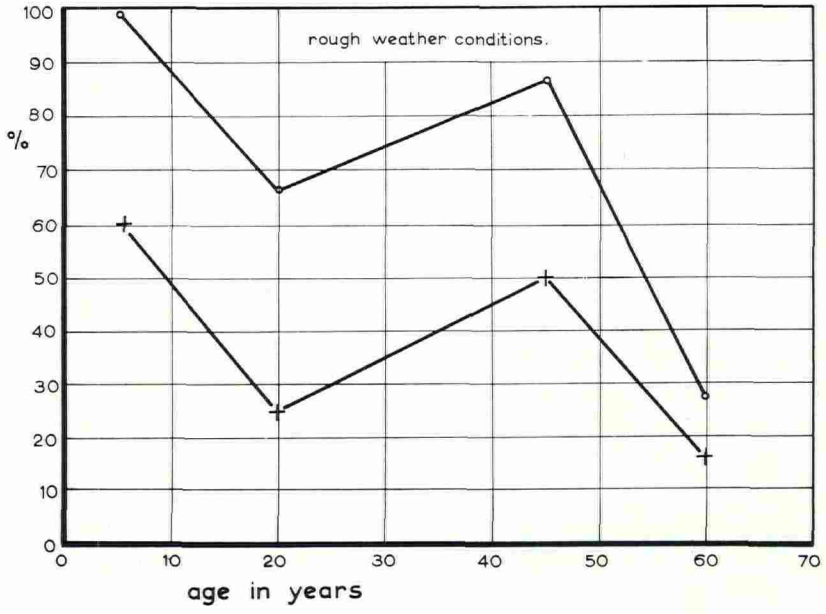


Fig. 29.

Percentage of passengers (male and female) seasick with (o) or without (+) drug.

The general tendency is that the female sex is more susceptible to the movement of the sea than the male. The sensitivities are in the proportion of 2 : 3 for males and females. It is further remarkable that young children and people around 50 years of age fall earlier victim to seasickness than persons of the other age groups. The best showing is made by the 60-year and older group. The high percentage among the 50-year group is probably to be attributed to the special condition of life in this group. Many of the men are living

under great stress and mental tension imposed on them by their occupation, or their family affairs or further social obligations. The women of this age are in the climacteric, and many of them are also exposed to more or less the same tensions as the men.

According to our questionnaire, the very young are even more sensitive to seasickness than the 50-year group. However, we do not wish to attach any great value to this conclusion, as the total number of children included was small (12) and the percentages are not statistically significant.

As regards the takers of drugs: the ratio of 73 % females to 37 % males shows that the number of females taking anti-seasickness drugs is nearly twice that of the males. It also appears that such drugs, e.g. dimenhydrinate (available commercially under the brand-names 'dramamine', 'suprimal' etc.) in general give little protection: of the 30 drug-taking males 22 were still seasick (70 %), while the 50 non-users yielded only 13 seasick (26 %). Among the women, 14 of the 30 non-users were seasick (about 47 %) against 70 of the 83 taking these drugs (about 85 %). This would appear to suggest that such drugs promote the development of seasickness. This, however, is doubtful for the following reasons.

1. The drugs are used by those who know from experience that they are very sensitive to motion sickness.
2. The drugs are presumably taken at a moment when the first symptoms of seasickness have already appeared, a moment when it is to be expected that the conditions are favourable for the further development of the condition. The important thing is therefore that the drug acts at the wrong moment. We can illustrate this in the following way:

In the schema given before (Chapter III) it was postulated that when the vestibular system is subjected to periodical stimulation, this system gives off trains of action potentials which, via the reticular substance, reach and stimulate the autonomic nervous system. In normal persons, however, an inhibitory and likewise periodical stream of action potential trains arises, and these compensate or antagonize the action of the vestibular system on the autonomic nervous system. This inhibitory flow originates from higher nuclear regions (probably somewhere in the corpus geniculatum).

Kliniek voor keel-neus-oorheelkunde der Rijksuniversiteit te Utrecht

Aan boord H.M.'s Holland	Datum 8-4-54
Naam A. J. Francken rang Matroos	Uitgereikt door Mw 2 Wormbrink
Onderdeel/bak	Stamboeknr.
	Leeftijd 27

Deze vragenlijst vormt een deel van een onderzoek naar zeeziekte. Het succes van dit onderzoek hangt voor een groot deel af van de nauwkeurigheid, waarmede U de vragen beantwoordt. Mogen wij daarom op uw medewerking rekenen?

De gegevens worden uitsluitend gebruikt voor wetenschappelijk onderzoek; zij zijn dus niet van invloed op uw conduite.

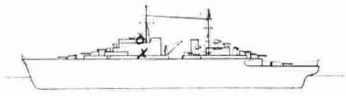
1. Hoe lang ongeveer hebt U in het totaal gevaren?	Over 5 jaar 4 reizen (duur) 2 dgn - 6 weken
2. Bent U gevoelig voor zeeziekte?	Jawel
3. Zo ja, bij welk weer treedt de zeeziekte op: reeds bij mooi weer met rustige zee, of resp. bij matige, ruwe of zeer ruwe zee? (S.v.p. hiernaast precies aangeven).	Matig ruwe zee
4. Bent U ook gevoelig voor wagen- of luchtziekte?	Wagen ziek niet, luchtziek wel
5. Hebt U ook op de wal wel eens last van duizeligheid of onzekerheid?	Neen
6. Hebt U ooit een hersenschudding gehad, zo ja, wanneer?	Neen
7. Hebt U wel eens een periode van ondervoeding (b.v. in krijgsgevangenschap, hongerwinter) gehad?	Nauwelijks
8. Hebt U, behalve de gewone kinderziekten, wel eens een ernstige ziekte (b.v. hersenvliesontsteking) gehad?	Neen
9. Wat is bij U het eerste symptoom van zeeziekte? (B.v. duizeligheid, misselijkheid, „flauw gevoel", *hoofdpijn etc.*)	Loomheid Transpireren
10. Als U flink zeeziek bent, hebt U dan last van:	
algemene slapte	7
angst	0
desoriëntatie	2
hoofdpijn	7
misselijkheid	10
depressie	8
duizeligheid	4
koud zweet	
diarrhoe	
(Al deze verschijnselen met een cijfer waarderen: 0 = geen last, 1 = iets last etc. tot 10 = zeer ernstig toe).	
11. Als de zeeziekte voorbij is (doordat U b.v. weer op de vaste wal staat) zijn dan alle verschijnselen verdwenen, of hebt U dan nog last van hoofdpijn, onzekerheid, „nadeinen" etc., en na hoeveel tijd verdwijnen dan deze verschijnselen?	Alle verschijnselen vrijwel onmiddellijk voorbij

Fig. 30.

Questionnaire handed out to the personnel of the Royal Dutch Navy.

VRAGEN DEZE REIS BETREFFENDE.

12. Uw kooi (nachtverblijf) bevindt zich op . . . . .
(In tekening aangeven met kringetje ○).
U hebt uw werk op . . . .
(aangeven met kruisje ×).



13. Wanneer begon U zich ook maar enigszins zeeziek te voelen? . . . . Geef zo nauwkeurig mogelijk datum/uur aan. (Invullen achter „a").	1e keer a 2-3-54 11 uur.
14. Wanneer bereikte de zeeziekte haar hoogtepunt? (Invullen achter „b").	b
15. Wanneer begon de zeeziekte weer te verminderen? (Invullen achter „c").	c
16. Wanneer was de zeeziekte geheel voorbij? . . . (Invullen achter „d").	d 4-3-54.
	2e keer a 15-3-54 17 uur.
	b
	c
	d 18-3-54
	3e keer a 2-4-54
	b
	c
	d 5-4-54
17. Hebt U middelen tegen zeeziekte ingenomen, zo ja, wanneer, welk middel en hoeveel?	Neen
18. Wat was het resultaat van dit middel?	

19. Indien U nog verdere opmerkingen hieraan wenst toe te voegen, gelieve U deze hieronder op te schrijven.

Aan een neiging tot misselijkheid gaat
vooral een sterke vochtafscheiding in de
mond

Fig. 30.
Questionnaire handed out to the personnel of the Royal Dutch Navy.

Because the drugs in general first exert their narcotic effect on the higher areas in an analogous way as in anaesthesia, a condition will first develop in which the inhibition is counteracted; thus the vestibular influence can be transmitted to the autonomic nervous system without being inhibited. In the following period the drug will also interrupt this connection; only at this moment, therefore, does the antiseasickness activity become a fact. In the presumably short interval in which the drug has only paralysed the inhibition, the vestibular influences will be promoted. Had the test subject taken the drug two hours before the onset of the seasickness, there would not have been such a period of facilitation. This is the reason why these drugs must be taken well beforehand, in order that they may be effective when the motion of the sea begins to make high demands on the central nervous system.

Connection between the various phenomena of seasickness

We were able to make a closer study of the connection between the successive manifestations of seasickness in another survey conducted by us among male personnel of units of the Royal Dutch Navy; these men did not use drugs. Here also a questionnaire form was used (see Fig. 30). A total of 635 forms were handed out, of which 630 were returned to us, all of them with data suitable for statistical analysis. On board these ships the accelerations caused by the movement of the sea were recorded with the 3D-accelerometer of GROEN, as well as with other types. These measurements showed that the sea was normal to calm during this voyage, so that there was no extreme stimulation of the organs of equilibrium, except for a short period in the Bay of Biscay.

In the first place we tried to identify the first indisputable symptom of seasickness in persons considering themselves normal (question 9). The answers were as follows: general malaise 32 %, headache 29 %, slight sensation of nausea 23 %, a feeling of disorientation 9 %, sialorrhoea 3 %, excessive sweating 2 %.

It is interesting to arrange the phenomena mentioned under question 10 in the sequence of their importance. For this purpose we tried to find out the correlation between these symptoms by means of the figures given by the subjects themselves. The coef-

ficients of regression were determined as a function of the tendency to vomit.

A good correlation was found to exist just before vomiting, with:

cold sweat	r = 1.0
headache	r = 0.65
dizziness	r = 0.56
general weakness	r = 0.55

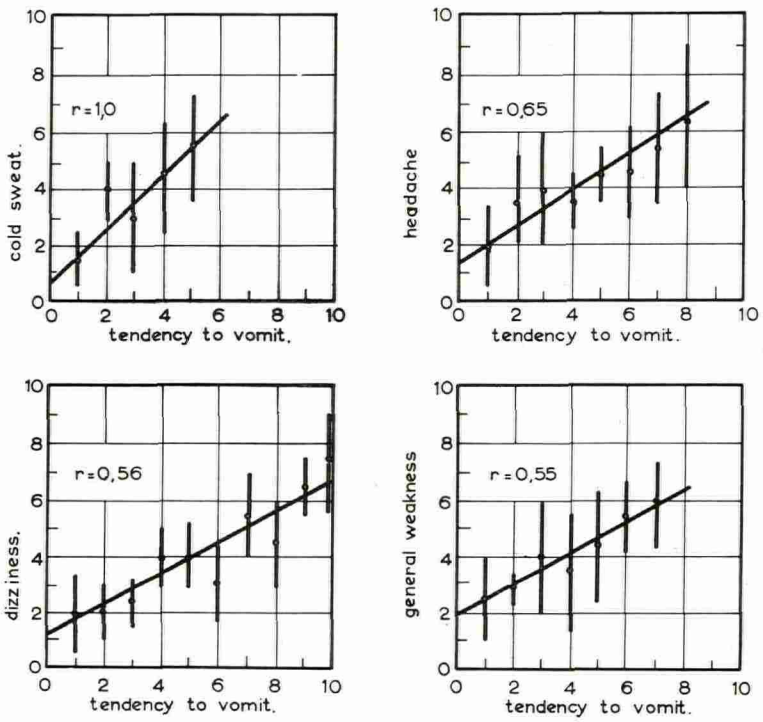


Fig. 31.

Correlation between the various symptoms as a function of the tendency to vomit.

It was further shown that the symptoms generally present were, in order of frequency: general weakness, headache, slight nausea, dizziness, sialorrhoea and cold sweat. They also preceded vomiting in this order. When the stage of vomiting had nearly been reached, the subject was usually feeling so ill that he was no longer able to

evaluate his symptoms according to their real intensity. This implies that as regards the higher figures for the tendency to vomit, there are practically no reliable data with respect to the evaluation of the other symptoms. Only as regards dizziness did the subjects know how bad their condition was, even when they vomited. For other symptoms no definite relationship was found, either with the tendency to vomit or mutually; for this reason we shall not pursue this subject further.

Comparison with the results of other authors

How do our results compare with those of other authors? In the first place we wish to compare them with the incidence of seasickness as given by HANDFORD, CONE and GOVER. During the first part of a sea voyage (2½ days) they studied the incidence of seasickness among 638 boys and men aged 17 to 35 years. The pitching and rolling of the ship was measured at various times, as were also the vertical accelerations at four places on board which were representative of places where the crew spent most of their time. The accelerometers were of the strain-gauge type, and the angular movements were measured with a gyroscope. While the average acceleration amplitude in the period observed was about 0.1 **g**, the number of seasick cases rose to 35.5 % of the total of persons. A number of men recovered during this period, however, so that the total percentage of men seasick at the same time was not higher than 25%.

The authors themselves state that the sea was very calm during this voyage. As the pitching period was on an average 5.8 seconds, while that of the 'Maasdam' was 7 seconds, the figures are not directly comparable. The change of acceleration per time unit was $\frac{7}{5.8} = 1.2$ as great for the warship studied by HANDFORD and co-workers.

The average acceleration amplitude of 0.1 **g** given by these authors is therefore comparable with 0.12 **g** in our measurements. The latter give a maximum of 10 % of cases of seasickness. This suggests that the longer night's rest of the passengers and their freedom to lie down in their cabins may cause our figures to compare favourably with those of a troop-transport ship. This seems to be confirmed by

a report that, on such a transport ship, most of the seasickness occurred a short time after reveille.

While HANDFORD and co-workers failed to find a correlation between the ship's motion and the percentage of seasickness, we were so fortunate as to be able to trace such a relationship (see Figs. 27 and 28).

Considerations on seasickness

After-effects

When the passengers disembark, the manifestations of the disturbance usually disappear rapidly. In spite of this, it seemed worth while to investigate whether there were persistent symptoms, what these were exactly and how rapidly they disappeared. Ten percent of the subjects of our investigation had definite after-effects. The majority of them (40 %) experienced an 'after-heaving', especially noticeable on the first night ashore. In 32 % of the patients a mild headache persisted. A mild feeling of nausea and disorientation was still present shortly after disembarkation in about 10 % of the patients, lasting for about two hours. The manifestations had disappeared in one day in the majority of cases (53 %). In 20 % of cases this lasted only two hours after disembarkation, but in another 20 % the symptoms persisted for two days. Practically all residual phenomena had cleared up after three days.

The after-symptoms such as headache, which seem to persist for two days or so, are of an autonomic nature. It is obvious that the body, the autonomic nervous system of which was seriously disturbed during the sea voyage, needs some time to reach the previous condition of balance again.

We shall now consider the other type of residual disturbance, the after-heaving, against the background of a successful or unsuccessful habituation to the movement of the sea. We are of the opinion that the after-heaving forms the inevitable conclusion of this habituation.

Habituation to the motion of the ship

We regard this habituation as a physiological activity belonging to the large group of the more general adaptations. We believe that

our case is particularly suitable for a closer study of adaptation phenomena, and that these can be based on a more general hypothesis, because this particular form of adaptation, the habituation to the movement of the ship can be divided into various stages.

The elementary processes underlying the adaptation can be studied by special experiments on the organs of equilibrium, as all manifestations of seasickness originate in these organs and their communications with and influences on the body. Let us therefore consider the reactions to a forced harmonic vibration.

We assume that the test subject, placed on a torsion swing with vertical axis (VAN EGMOND, JONGKEES and GROEN, 1949), his head somewhat bent forward, is subjected to the oscillation of the swing. The swing is turned into a starting position and then released. The resulting movement is a damped harmonic vibration. What, then, are the sensations this test subject experiences? He feels the oscillation very clearly, even so accurately that the natural period of his horizontal canals can be calculated from his indications regarding the supposed turning points of the swing. However, towards the end of this decaying movement he sometimes has the clear impression that he no longer oscillates alternately to the left and to the right, but that, for example, he skips a movement to the left, or in other words, that he feels two successive sensations of movement to the right. This may be followed by a period of two or more successive left-sensations. This phenomenon, also observed and described by VON BEKESY (1955) must be of central origin. There is no analogon in the peripheral organ like that studied by GROEN, LÖWENSTEIN and VENDRIK in the ray. According to these authors, the peripheral organ behaves, at any rate insofar as can be measured, like an ideal damped torsion swing. In this case the peripheral organ sends out a train of action potentials to the centres, with a sinusoidal frequency modulation. The amplitude of the modulation decreases proportionally to that of the torsion swing. No particular deviations have ever been observed for the small movements. This leads to the conclusion that the abnormal sensations observed must be of central origin.

What central mechanism forms the basis of this? *We assume that on continuous systematic stimulation of the central nuclei, a duplicate of this stimulus is formed; this copy originates in the higher*

centres, is conducted towards the lower centres via the efferent pathways, and is deposited in an associated accessory nucleus as well as in the afferent nucleus concerned. That this may be possible is shown by the experiments of ERICH VON HOLST and co-workers with animal experiments. In a publication of this group (VON HOLST and MITTELSTÄDT, 1950) it is demonstrated that there exists a copy of the stimulus resulting from an intention; this duplicate is deposited in the accessory mucleus of the group of nuclei destined to receive the re-afference of the result of the intention.

The schema shown below is reproduced from the work of these authors.

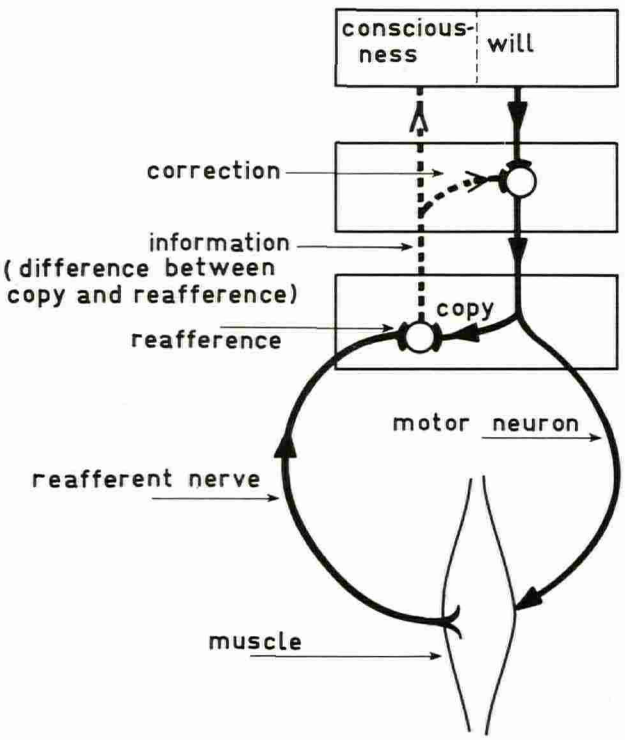


Fig. 32.

Reafference principle (VON HOLST) as demonstrated in the case of a voluntary muscle.

To effect the contraction of the muscle drawn in the above schema, a signal is sent down from the cortex. The muscle contracts, information of which contraction is sent via the afferent pathway starting from this muscle towards the lower nucleus (for example situated in the medulla oblongata). However, the efferent pathway gives off a branch to the same nucleus, in which the intention to contract was deposited in duplicate form. If duplicate and re-afference are identical, the muscular contraction evidently took place in the correct way. In the opposite case, there is a difference between copy and re-afference, which difference is fed back to the higher nuclei, where there exists the possibility of interaction of this information with the original efference, so that finally the muscular contraction is completely carried out in the correct way. The authors substantiate this ingenious new conception on reflexes and cybernetics by many examples of animal experiments.

The interesting fact for us is that a command given in the form of action potentials can be stored away, for example in the form of specific chemical energy. The later returning re-afference, also consisting of trains of action potentials, is converted in this nucleus into specific chemical energy, at any rate in an analogous form, which must be the counterpart of the copy. The muscular contraction, i.e. a movement, can evidently be projected in a suitable way on the central nervous system, and this projection must be so exact that it is completely comparable and even interchangeable with the duplicate, and conversely. Duplicate and re-afference are comparable forms of the projection of a series of actions. Viewed from this angle, the periodic stimulation of the organs of equilibrium might give rise to the construction of a duplicate condition, caused here by the original afference and the subsequent afference to the hypothetical copy nuclei. After prolonged periodical stimulation a copy of the expected movement has been built up. If the stimulation had not lasted long enough, the copy would not yet have been perfect in all respects.

The test subject on the decaying torsion swing is in this position: The duplicate has not yet been laid down firmly, especially as regards the phase. The decaying movement gives off a continuously weakening series of signals. The copy, which had initially started correctly, becomes weaker and is no longer in phase with the

projection of the real movement. This wrongly-acting interference creates a brief period of silence, preceded and followed by, for example, a rotatory movement to the right, the left turn being suppressed by the interference. The whole picture acquires to some extent the character of beats between real and supposed (or duplicate) vibrations.

When what is said above is applied to the more complicated motion of the sea, the following picture might arise. The habituation lasts about three days and the dehabituation about a day. When, with respect to pitching, the ship's movement is regarded as beats with a period of about 40 seconds, in which about 6 or 7 oscillations take place, the central nervous system must have ample occasion to build up a copy of this. This can of course never be a completely finished one; on the contrary, it will have to be adjusted from moment to moment (especially as regards the phase): the movement of the ship never repeats itself exactly. The duplicate model of such beats of positional movements is, as a whole, about complete, but the moment at which this copy can be placed against the projection of the real movements may be postponed by information obtained from the external world. After three days (the period of habituation) a good imitation of the presumptive ship's movement has therefore been built up. This copy is so effective that the equilibrium-restoring corrections of trunk and extremities can for the greater part be regulated by the duplicate under guidance and trimming by the projection of the external stimulus. When this is achieved, the person is adapted.

When the external stimulus stops, the copy is left. We know that after-heaving is one of the most frequently occurring after-sensations of the sailor. This after-heaving must be considered a direct result of the persistence of the copy. There is not only the after-sensation of heaving, but body and extremities keep receiving impulses from the copy; the person makes a sudden side-step in the corridor of the hotel he went to directly after the end of the sea voyage. The walls of the corridor move as if the hotel were making the same rolling movement as the ship did before. The dehabituation usually takes a day, but there are many persons who after three days still occasionally feel the 'heaving of the ship' in bed. The attractive aspect of this hypothesis is that the copy is as real as the projection of the

real movement; not only as regards the sensations, but also with respect to the cybernetic functions which otherwise are completely the domain of the organ of equilibrium (GROEN, 1957).

Although up to now we have been dealing with short-term habituation, it may also be of interest to investigate habituation over a long period. It is known from the experience of many generations of seamen that in general the persons with the greatest number of hours at sea are the least troubled by the ship's movement, even when the voyage is repeatedly interrupted.

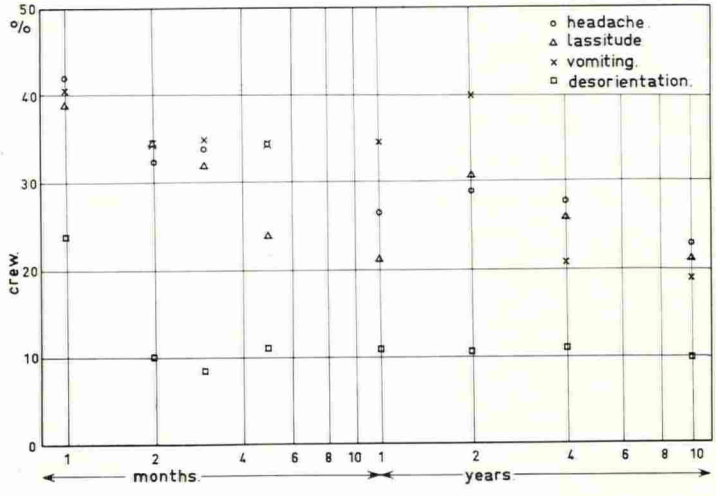


Fig. 33.

Adaptation to the various symptoms of seasickness as a function of number of sea hours.

For this purpose the more than 600 questionnaire forms were arranged according to the number of sea hours of the naval personnel interrogated and the ever-returning unpleasant symptoms were studied. It was indeed found that the tendency to seasickness decreased with increase of the number of hours at sea. While of the younger personnel only 20 % ended the voyage without seasickness, 55 % of the older men (with three or more years experience at sea) underwent the ship's movements without symptoms. Fig. 33 gives a graphic representation of the frequency of headache, fatigue, nausea and disorientation, as a function of the time spent at sea, with normal

interruptions. The incidence of excessive sweating (2 %), hunger sensation (1.5 %) and sialorrhoea (1 %) was too low to give valid indications regarding habituation.

Some habituation is evidently present after the first month at sea. The average period needed to become an experienced sailor is about four years; then fatigue and headache are the main residual symptoms in, on an average, 25 % of the subjects.

As experience increases, the disorientation and the feeling of uncertainty persist in only 10 % of cases. After an initial fall from 40 % to 35 %, the feeling of nausea, as manifest extreme symptom, remains for a long time. Only after four years does it become clearly less, to decrease subsequently to 18 %.

The specifically seasick subject

As a normal person needs three days to become adapted to the motion of the ship (on a normal sea) the problem arises of the difference between normal persons and those who cannot become accustomed to even the slightest movement.

What objective data can be obtained from the examination of a person who is very sensitive to motion sickness?

There are only few exact data available, and these have been obtained with the help of cupulometry. In his monograph *Seasickness* (1953) DE WIT shows that there are two kinds of measurable variables, which differ in seasick persons and in normals, provided all further medical examinations absolutely exclude any other abnormalities and the past history does not mention any abnormality either. Here we are therefore dealing with a group of otherwise perfectly healthy people who have only one abnormality in common: hypersensitivity to continuous changes of movement or, briefly, liability to motion-sickness. The first variable is the retinal blood pressure. This is measured with the ophthalmodynamometer of BAILLIART and is expressed in BAILLIART units. When normal persons and seasick persons are subjected to the same sinusoidal linear acceleration (parallel swing), both have a raised retinal blood pressure after a certain number of oscillations. Seasick persons however show a much greater rise than normal persons.

Although this phenomenon gives a direct indication of the

coupling between vestibular stimulus (otoliths) and the autonomic nervous system, the measurement is very difficult to carry out as a routine investigation. It requires great skill on the part of the observer to obtain reproducible results over a long time.

The second method to determine the degree of sensitivity to motion sickness is supplied by cupulometry. The normal cupulogram shows a different slope for duration of sensation and duration of nystagmus, on an average 8 seconds and 12 seconds, respectively. This peculiarity, which is the expression of a discrepancy, has led to the hypothesis of the central inhibition of activity in the higher vestibular nuclei (see Chapter III on Physiology and Anatomy). This phenomenon of a non-parallel course was shown by all normal test persons. There is however a small group of persons with otherwise normal health who do show a parallelism in the course of sensation and nystagmus. All persons belonging to this group are characterized by a manifest tendency to motion sickness. The greater the sensitivity to motion sickness, the longer the times of decay, and the steeper the slopes in the cupulogram. Values of 25 seconds for sensation and nystagmus are even found (Fig. 11). At the time GROEN calculated that the decay-constant of a semicircular canal would have to be about 25—30 seconds, so that in the case of seasickness we are dealing with a pure reproduction of the stimulated condition of the peripheral organ in the central nervous system. Although in the seasick we are mainly dealing with the influence sphere of the otoliths, for which we must assume a certain uninhibited transmission of the otolith activity to other regions of the central nervous system, there appears to exist a quite analogous situation for the semicircular canals. It follows from this that sensitivity to seasickness largely means uninhibited transmission of the activity of the whole vestibular organ to the other regions, so that a disposition to seasickness can just as well be measured with the help of the semicircular canals as with the otoliths.

A normal person is able to limit the vestibular influence to the equilibrium-reflex system, in which the transmission to other regions can mainly be suppressed autonomically, in so far as required. It was also shown in normal persons who, as regards equilibrium, live under abnormal daily conditions, that a much more far-reaching inhibition is even possible. Proof of this is rendered by the fighter

pilots examined by KRIJGER. This also shows that the inhibition is not a constant factor, but is adapted to the conditions of living of the test person.

The incapacity to achieve inhibition marks the test person as a potential victim of seasickness. He remains a puppet in the hands of his own vestibular system.

The non-specifically seasick

DE WIT (1953) makes a distinction between the specifically and the non-specifically seasick; the latter category comprises those who have an acquired sensitivity to seasickness. He arrives at this distinction after an accurate analysis of the anamnestic data. A great number of the general group of seasick persons had a similar past history. Many of them had suffered a concussion, while others had developed an increased reaction to forced movements after an infectious disease, either of bacillary or of viral nature. After influenza, especially, there is a risk that a person of the normal group may join the group of the non-specifically seasick. All the categories mentioned have a common background, namely a disturbance of the regulation acting from the higher centres on the lower ones. Concussion has as well-known sequelae all kinds of slight disturbances of the dynamic equilibrium in various functions (headache), while influenza gives rise to encephalitic side effects, which, as residual condition, leaves behind the same disturbance in the dynamic equilibrium. Especially the descending pathways, which would appear to effect the inhibitions, seem to be most disturbed in their beneficial functions. Again viewed from the standpoint of the inhibitions, it is understandable that then a predisposition to seasickness has been created. DE WIT demonstrated these hypotheses on some cases in an illustrative way.

CHAPTER VIII

FINAL CONSIDERATIONS; CONCLUSIONS

The preceding chapters dealt with the relationship between the ship's motion and the phenomena of seasickness. It is shown that the rate of change of the vertical acceleration forms the stimulus for the production of these manifestations. The point of action of the movement of the ship on human beings appears to be the organs of equilibrium, in particular the otolith. Our measurements showed that a change of acceleration of 1 m/sec^2 per unit of time is tolerable for a sea voyage longer than three days; only 10 % of the passengers will react to it with lasting symptoms of seasickness. When the rate of change of the vertical acceleration increased to 2.5 m/sec^3, the physiological limits of the adaptation were exceeded in a great number of passengers, 20 % of them being chronically seasick.

It is interesting to compare these data with those obtained in a quite different way, namely from the study of the disagreeable vibrations caused, for example, by transport vehicles. In 1931 REIHER and MEISTER evolved criteria for the degree of discomfort caused by vibrations of various frequencies, like those produced in trains, motor cars, aircraft and other means of transport. The shaking of houses in the immediate neighbourhood of machines which impart heavy shocks to the ground was also included in this investigation. Although the criteria for this kind of discomfort differ to some extent from those which might be evolved for the movement of a ship, there are undoubtedly points of correspondence between these different movements. In the first place the thresholds can be compared, for which we use the curves of REIHER and MEISTER, supplemented by BONJER and GROEN (see Fig. 34). These curves show, as a function of the frequency, the acceleration per cm/sec^2

causing a particular degree of discomfort. The whole range is divided into five zones, in order to obtain a rough classification. The threshold curve can be divided into three areas:

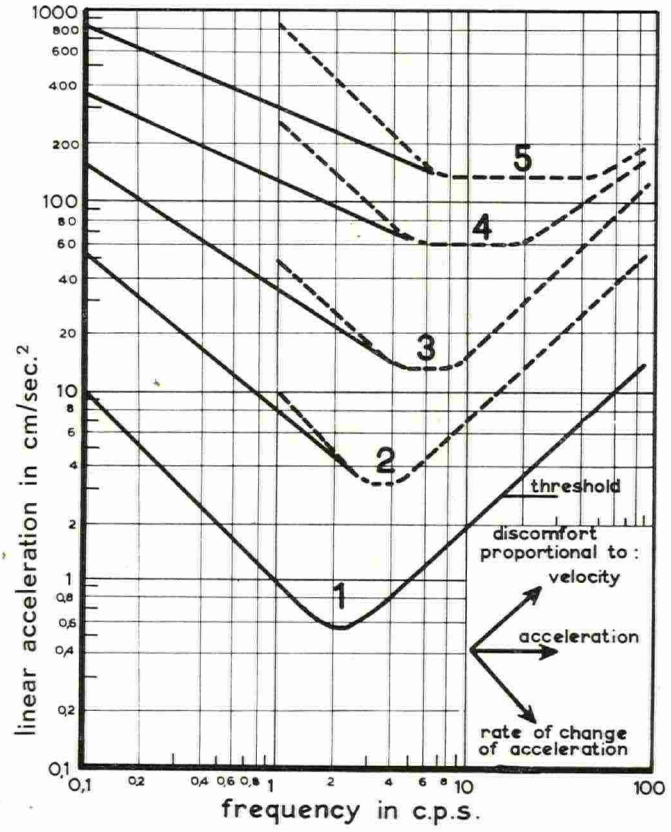


Fig. 34.

Influence of vibration on human discomfort.

- - - - - REIHER and MEISTER.

———— Proposed curves by Neth. Working Committee (1954).

Zone 1: just perceptible.

„ 2: clearly perceptible.

„ 3: strongly perceptible, beginning of discomfort.

„ 4: decidedly unpleasant.

„ 5: unbearable.

a. a low-frequency part up to 2 cps, comprising practically all ship's movements for which the stimulus is proportional to the rate of change of the acceleration;

b. a resonance-like inflection in the neighbourhood of 2 cps, later rising to 10 cps for stimuli of greater intensity, in which the magnitude of the acceleration is decisive for the intensity of the stimulus.

c. a part higher than 2 cps (later higher than 10 cps), where the stimulus is proportional to the velocity.

The fact that the whole range is not dominated by the rate of change of the acceleration is probably due to resonance phenomena of the head with respect to the trunk at 2 cps, so that for higher values the picture changes in the sense of a relationship dependent on velocity. However, the field below 1 cps, which is of importance for our subject, shows clearly a character fully dominated by the action of the otoliths: the rate of change of the acceleration is decisive for the reaction of the test subject, as clearly demonstrated by the threshold curve. The tolerable 1 m/sec^3 and the absolutely disagreeable 2.5 m/sec^3 appear to fit logically into the collection of curves extrapolated by BONJER and GROEN. That the curves of zones 4 and 5 are flatter than near the threshold can probably be explained from the exceeding of the physiological limits of tolerability.

At any rate, the manifestations of seasickness and the discomfort caused by vibration belong to one large group, the low-frequency range of which is completely dominated by the otoliths. The phenomena of vibration discomfort appear to correspond with those observed in seasickness, for example lassitude, aversion from work, headache, cold sweat, bradycardia, etc.

The coupling of the vestibular nuclei to the autonomic nervous system, presumably via the intermediary of cerebellum, reticular substance and hypothalamus, is responsible for the phenomena mentioned. This coupling is liable to be influenced by an inhibiting action, but a chronically seasick person is powerless to exert any regulating influence on this coupling. The anti-seasickness drugs prevent the coupling, after first having decreased the mitigating action in the inhibiting descending pathways. In the transitional phase during the use of anti-seasickness drugs, when the inhibition is already intercepted but the coupling seems to persist in an even less inhibited

form before it also becomes suppressed by the drugs, the latter facilitate the development of seasickness.

The hypothesis of the adaptation process has been evolved on the basis of the after-sensations experienced after disembarkation, especially the after-heaving. The adaptation to the complicated ship's movement is attained in about three days, and is regarded as a central construction of a copy of the projection of the ship's motion in the central nuclei, brought about via the organs of equilibrium. The duplicate possesses all properties of a neural activity, as if it were a real external stimulus. This copy persists for some time after the causative external stimulus has stopped. The after-heaving is a direct result of this duplicate activity. Practically everybody seems to possess this ability to adapt, as shown, for example, in centrally curtailed reactions of vestibular nature, such as nystagmus and sensations.

The category of the persons who have a tendency to seasickness, but are normal in all other respects, does not seem to possess this ability to inhibit, as evidenced by the non-curtailed vestibular reactions. The ability to adapt is probably firmly associated with the power of inhibition; absence of the latter is accompanied by absence of the former.

CHAPTER IX

SUMMARY

Seasickness is considered here from the following points of view:

a. *Mechanical stimulus.* During several sea voyages records were made of the accelerations of the ships on board of which the investigation was conducted.
b. *Frequency of seasickness.* The incidence of seasickness was studied by means of questionnaires issued to all persons on board these ships.
c. *Symptomatology of seasickness.* The severity of the phenomena and the sequence in which they occurred were noted by passengers and crew on the question forms.
d. *Influence of age, sex, number of preceding hours at sea and the use of anti-seasickness drugs* were also covered by the questions on the forms.

These data show that the average person needs an average of three days at sea to get habituated to the normal ship's motion, in which the rate of change of the vertical linear acceleration should not exceed 1 m/sec^3; this value can be considered permissible for a comfortable sea voyage. Under these conditions 10 % of passengers at most will be seasick during the first three days. A much lower percentage (about 2 %) will remain seasick during the whole voyage.

On a rough sea, on which the ship is subjected to changes in vertical acceleration of 4 m/sec^3, 30 % of those on board are chronically seasick, while the other 70 % still become adapted in three days.

This condition of adaptation disappears relatively soon, in one day, when the passenger goes ashore; in some people however, its influence can still be observed after three days. The residual symptoms are headache and after-heaving.

It appears from the symptoms preceding vomiting that the vestibular stimulation first causes a sympathicotonic phase, followed by a parasympathicotonic one, as shown by the succession of the symptoms which culminate in the nausea syndrome.

Based on the neural communications of the vestibular organs with the hypothalamus, running via cerebellum and reticular substance, the coupling of the vestibular system to the autonomic nervous system is shown to be probable.

The adaptation process is considered as a central construction of a duplicate stimulation according to the reafference principle of VON HOLST, in which adaptation and inhibition are regarded as closely related manifestations. All this is supported by observations on groups of chronically seasick subjects; the lack of inhibition and the inability to achieve inhibition in this group are clearly demonstrated.

Females are in general more sensitive to the ship's movements than males (3 : 2). The most susceptible age is that about 50 years, when men are usually under excessive stress imposed on them by their busy lives, while the women are in the climacteric period. The age group most resistant to seasickness is that above 60 years.

The anti-seasickness drugs only have a favourable effect when they are used in the correct way, and even then their usefulness is relatively limited. The ingestion at the right moment, i.e. 2½ hours before the expected increase of movement, is too often forgotten. When this excessive motion has already begun before the drug is taken, the drug facilitates the development of seasickness. This is supported by arguments on the basis of the inhibition mechanism.

Seasickness belongs to the larger category of motion sickness, which also must be taken to include the conditions caused by vibrations of higher frequency, e.g., the discomfort caused by quasi periodic movements of trains, motor cars etc. It appears that the values given by us for tolerable and definitely untolerable ship's movements fit in logically with the criteria for vibration discomfort

known from other fields. Here also the otoliths form the points of attack for the vibratory discomfort, at any rate in the frequency range below 2 cps.

In view of these results, seasickness is to be regarded as an overstimulation syndrome resulting from an overalarmed and alarming reticular substance.

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