5. Special Senses

5.1 Vision

Anatomy of the Eye

The eye is a hollow sphere, the periphery of which is composed of three layers - a tough *outer* fibrous layer (the *sclera* and *cornea*), a *middle* layer comprising the vascular *choroid*, the muscular *ciliary body* and the *iris*, and an *inner* neural layer, the *retina*. The two inner chambers of the eye contain the *aqueous humor* and *vitreous humor* and suspended between them is the *lens*. The shape of the eye is maintained by an intraocular pressure of around 15 mmHg.

Image Formation

The stimulus for vision is electromagnetic radiation with wavelengths in the range of 400 to 700 nanom, detected by the receptors in the retina. Light which bypasses the receptors is absorbed by the pigment epithelium on the outer surface of the retina and the choroid layer. For sharp vision the eye must focus the light rays onto the retinal receptors and for the most detailed vision onto the region of highest acuity, the *fovea centralis*.

Focusing the Image on the Retina

When focusing for infinity the eye has a total converging power of about 60 dioptres (power in diopters = 1/focal length in m). Most of this converging power is achieved by the refraction of light rays at the curved air-cornea interface. The lens provides further converging power as well as the increase in power required for focusing objects closer than infinity.

The changes involved in looking from an object at infinity to one nearby comprise the *near response*, which has three components:

1. *Accommodation.* This is the increase in refractive power of the lens (maximum about 12 diopters) achieved by increasing the curvature of its anterior and posterior surfaces (particularly anterior). When focused for infinity, the lens is pulled flat by tension in the *zonule* (lens ligament). Accommodation is achieved by contraction of the ciliary muscles which are under the control of parasympathetic nerve fibres (CN III). This causes slackening of the zonule and releases the lens from tension, allowing it to round up due to its own elasticity.

2. *Constriction of the pupil.* This provides a better depth of focus, since with constriction light rays pass through only the central part of the lens. This reduces spherical and chromatic aberrations, which are caused by the aspheric shape of the cornea and lens and the higher refractive index of the lens core compared with its outer layers. Pupil size is controlled by both sympathetic and parasympathetic fibres to the muscles of the iris. Sympathetic fibres (cervical sympathetic nerve) contract radial muscle and thereby *dilate* the pupil; parasympathetic fibres (CN III) contract circular muscle and thereby *constrict* the pupil.

3. *Convergence of the eyes.* This ensures that the light rays from an object fall on corresponding parts of each retina thus giving a fused image. It is achieved by contraction of the two medial recti muscles controlled by CN III.

Defects in Focusing

There are three kinds of refraction error that occur in eyes, namely *hypermetropia, myopia* and *astigmatism.* Another defect in focusing is *presbyopia* in which there is a loss of accommodative power.

1. *Hypermetropia* (long-sightedness). In this condition the eyeballs is too short (or the focusing system too weak) and even with full accommodation objects nearby are focused behind the retina. This can be corrected by using a *convex* lens.

2. *Myopia* (short-sightedness). The eyeball is too long (or the focusing system too strong) and even with full relaxation objects at infinity are focused in front of the retina. This can be corrected by using a *concave* lens.

3. *Astigmatism.* Here the curvature of the cornea (or occasionally the lens) is not uniform, thus giving different degrees of refraction in different planes. Therefore the image is in focus in some planes and blurred in others. This can be corrected by using a *cylindrical* lens which gives additional refraction in the required meridian.

4. *Presbyopia*. The *near point of vision* is the distance between the eye and the closest object which can be brought to a clear focus. It recedes with age, being approximately 10 cm from the eye at 20 years and 80 cm at 60 years. This change is due to a reduction in the elasticity of the lens which decreases its ability to accommodate.

Light Reflex

The pupil reflexly constricts when looking at near objects or in response to light. There are two light reflexes - the *direct* and the *consensual.* When light is shone into one eye the pupil constricts and this is called the direct light reflex. At the same time the other pupil also constricts and this is called the consensual light reflex. The afferent pathway for the light reflex is via the optic nerve to the pretectal region of the mid-brain and the efferent pathway is along parasympathetic fibres of CN III.

Eye Movements

The two eyes may be moved in the same direction (conjugate movements or versions) or in opposite directions (disjunctive movements or vergences) as occurs for instance during accommodation. Eye movements are also distinguished as *saccadic*, the fast step-wise movement employed when altering fixation, and *smooth pursuit*, the movement employed when the eyes follow a moving object. A *squint* occurs when the visual axis of one eye is not fixed on the object being viewed by the other.

Receptor Mechanisms of the Eye

Receptors

There are two kinds of receptors, *rods* and *cones.* They are located at the back of the retina, furthest from the entering light rays and next to the pigmented choroid which absorbs stray light and thus prevents blurring.

Rods

120 x 10^6 per eye. They are not found in fovea but are dispersed throughout the rest of the retina. Have high sensitivity and are used in night vision. They have poor acuity. They do not give colour sensation.

Cones

7 x 10^6 per eye. They are highly concentrated in fovea, and less concentrated peripherally. Have lower sensitivity and are used in day vision. Have high acuity, especially in fovea where limit is diameter of one cone (2-3 microm). They give colour sensation.

Photopigments

Light is detected by its reaction with photopigments located in the receptors. Each photopigment consists of a protein, *opsin,* and a chromophore, *retinal* (the aldehyde of vitamin A). There are four forms of opsin giving four photopigments - the rod photopigment, *rhodopsin,* (maximum absorption 500 nanom), and the three cone photopigments, *erythrolabe* (maximum absorption 565 nanom), (red-sensitive), *chlorabe* (maximum absorption 540 nanom), (green-sensitive) and *cyanolabe* (maximum absorption 440 nanom), (blue-sensitive). The ability to detect different colours results basically from different degrees of excitation of the three cone types.

The brightness of light depends on its wavelength and on whether the eye is adapted for night vision (*scotopia*) or day vision (*photopia*). The scotopic spectral luminosity curve has a peak at 507 nanom and is characteristic of the absorption spectre of rhodopsin, while the photopic spectral luminosity curve has a peak at 555 nanom and is characteristic of the absorption spectra of the three cone pigments combined. Thus in scotopic vision the eye is most sensitive to green while in photopic vision it is most sensitive to yellow. The shift from scotopic vision to photopic is called the *Purkinje shift.*

The effect of light on the photopigments is to isomerize thee chromophore retinal and hence to start a series of reactions in which a number of intermediate compounds are formed. The reactions lead eventually to the splitting of retinal from opsin, a process known as 'bleaching'. The series of reactions is associated with a potential change across the plasma membrane of the receptor cell known as the *early receptor potential.* This potential is not usually recorded in the electroretinogram (ERG) unless high stimulus intensities are used. However, if present, the amplitude of the early receptor potential can be used as an estimate of the amount of photopigment present.

Adaptation

The sensitivity of the eye is dependent on the ambient light intensity. On going from a light environment into a darker one there is a gradual increase in sensitivity allowing dimmer lights to be seen, a mechanism known as *dark adaptation.* This is due to pupil dilatation and to changes in receptor sensitivity. The latter has two components - an initial one involving cones and a later one involving rods. The final stage in sensitivity is about 10^5, of which only a small fraction is due to dilatation of the pupil and most to regeneration of photopigment and to neural mechanisms within the retina, occurring over approximately 30 min.

A much faster (3-5 min) period of *light adaptation* occurs when going from a dark environment into a brighter one, which results from pupil constriction and bleaching of photopigments.

Receptor Potentials

The bleaching of photopigment which results in the early receptor potential is followed by a change in permeability within the receptor which results in a *receptor potential.* Unlike most receptor potentials, which are depolarizations, this is a hyperpolarization, i.e., the inside of the membrane becomes more negative. It results from a decreased permeability to Na ions which reduces the steady current flowing through the receptor cells. The hyperpolarization is though to reduce the release of transmitter, which is occurring continuously, thus affecting the activities of other cells in the visual pathway.

Electro-Oculogram and Electroretinogram

There is a steady potential difference of about 6 mV between cornea and the fundus (posterior portion of the interior of the eye) generated predominantly across the pigment epithelium. As a result of this potential difference between the front (positive) and back (negative) of the eye, electrodes placed on the skin at each side of the eye detect a change in potential when the eye is moved in a horizontal direction. The record so obtained during eye movements is called an *electro-oculogram (EOG).*

Illumination of the eye causes a series of smaller changes detected between an electrode on the cornea and an indifferent electrode. This is known as an *electroretinogram (ERG).* The first part of the ERG reflects electrical activity within the receptors. It is due to permeability changes and associated ionic fluxes and should not be confused with potential changes in other cells within the retina and pigment epithelium.

After-Images

Visual sensations outlasts the stimulus and give rise to both *positive* and *negative* after-images. When an object is viewed briefly it continues to be seen as a positive after-image. However, with more prolonged exposure it appears as a negative after-image, i.e., a light source appears dark against a brighter background. If the light is coloured the negative after-image is tinged with the complementary colour. The minimum frequency required to

give a non-flickering picture is known as the *critical fusion frequency*. It is around 30 to 50 Hz and is higher at higher light intensities. Modern projectors work well above this (72 Hz) so that no 'flicks' are experienced.

The Visual Pathway

Retina

The retina is a complex outgrowth of the CNS and contains, besides the receptor cells, four other types of neurones - *bipolar cells, ganglion cells, horizontal cells* and *amacrine cells.* The rodes and cones (total about 130 x 10^6) synapse with bipolar cells which in turn connect to ganglion cells, whose axons (about 1 x 10^6) leave the eye at the *optic disc* to form the *optic nerve.* Thus there are about 130 receptors to each optic nerve fibre, although cones from the fovea centralis have far less, if any convergence. Horizontal cells connect receptor cells to each other while amacrine cells provide cross-connections between ganglion cells. The retinal cells are all arranged in orderly layers with the receptors next to the pigment epithelium and the axons of the ganglion cells running over the surface of the retina. As a consequence light has to first traverse these layers before reaching the receptor cells. At the fovea, where visual acuity is greatest, this orderly layering is modified; it contains mainly cones with the other neural elements displaced to the sides.

Central Pathways

Axons of the ganglion cells travel in the optic nerve and end in that part of the thalamus called the *lateral geniculate nucleus.* Fibres of the geniculate cells travel to the *primary visual cortex* (also called striate cortex and area 17) of the occipital lobe. There is a partial crossover of the optic nerve fibres. Fibres from the nasal halves of the retinae cross while those of the temporal halves remain ipsilateral, so that visual stimuli in the left half of the visual field of both eyes excite the right visual cortex and vice versa. Throughout the visual pathway the organization of responses is topographic with a particularly large representation of the fovea in the primary visual cortex. Visual information is passed on from the primary to other areas such as the peristriate cortex (areas 18 to 19) and inferotemporal cortex, and to subcortical regions (i.e., thalamus, mid-brain). Optic nerve fibres also provide an input to mid-brain pretectal regions and the superior colliculus which are involved in light reflexes and control of eye movements.

Neural Responses in the Visual Pathway

More is known about the responses of cells in the visual pathway than about cells in any other sensory system. Most of our understanding comes from experiments on animals in which recordings were made from nerve cells in the visual cortex and the most effective stimulus for each cell was determined. The results of this work carried out, especially by D. H. Hubel and T. N. Wiesel, in experiments dating from the 1960s, give what is perhaps the closest analysis of neurophysiological events in consciousness. It will be seen that particular aspects of the visual stimulus such as contrasts are selected. Thus constant levels of illumination are relatively ineffective as stimuli while changes in intensity with time or position are readily detected.

Responses in the retina. The complex interconnections and convergences which occur within the retina provide for considerable modification of responses to visual inputs between receptors and ganglion cells. Each ganglion cell in the retina receives inputs from receptors over a larger or smaller area of retina, which is called the *receptive field* of that ganglion cell. Most ganglion cells fire spontaneously even in the dark. This background activity can be changed by shining a small light spot within the receptive field. If the firing rate increases, this is called an 'on' response, if it slows, an 'off' response. When a number of ganglion cells are tested in this way, they fall into two groups. In the first, the receptive field is made up of a small more-or-less circular 'on' area surrounded by a larger ring-shaped 'off' zone, and these are called *'on' centre fields*. The second group has the converse arrangement: an 'off' centre field surrounded by an 'on' ring and these are called *'off' centre fields.* Some fields may have an intermediate zone in which both 'on' and 'off' discharges are recorded. The intensity of a response, that is, the amount of increase or decrease of discharge frequency, depends on how much a given area is stimulated. A process of summation is at work, so that the biggest response occurs when the stimulus spot covers the entire centre field. But if the stimulus spreads into the surround area there will be a tendency for the two effects, of different signs, to cancel. Thus, a stimulus just covering an 'on' area will give a large increase in discharge frequency but, if it is made bigger and spreads into the 'off' surround, the increase in discharge frequency will, in fact, be smaller. Consequently uniform illumination of the whole field is relatively ineffective.

The horizontal and bipolar cells show the beginnings of enhancement of spatial contrasts. Like rods and cones, horizontal and bipolar cells do not generate impulses but give slow hyperpolarizing and depolarizing potentials. The receptive fields of the bipolar cells show opposing effects between centre and periphery, presumably due to excitatory and inhibitory connections from different receptors. The pathway for such lateral inhibition appears to be via the horizontal cells. Amacrine cells are the first neurones in the visual pathway to generate impulses. They respond with a transient potential at onset and offset of illumination, rather than continuously, and thus may be important in the detection of moving stimuli.

In summary, analysis of the responses of retinal nerve cells shows that they do not simply relay all signals unchanged to the next cell in line, but that due to convergence and lateral inhibition the first stage of *integration* is taking place in the visual system. The receptors of adjacent areas combine their effects so that the ganglion cell discharges in a way determined by the relation of the intensity of illumination of the centre of its field to that of the surround.

Responses in the lateral geniculate nucleus. Axons of the retinal ganglion cells travel on to synapse with cells in the lateral geniculate nucleus of the thalamus. These cells have many of the characteristics of ganglion cells but their stimulus requirements are more stringent. They have receptive fields with 'on' or 'off' centres but, unlike a ganglion cell which can be stimulated by overall illumination of the retina, a lateral geniculate neurone can only be stimulated by some difference of illumination intensity between its field centre and its surround. Thus they respond only to contrasts within their own fields and movement of the stimulus produces a stronger response.

Responses in the visual cortex. Axons of the lateral geniculate neurones travels as the optic radiation to the visual cortex. Within the visual cortex most cells respond best to rectilinear contrasts between light and dark, such as slits, edges and lines, rather than circles. Most show a poor response or complete unresponsiveness to diffuse illumination. Cortisol cells have been grouped into classes called 'simple', 'complex' and 'hypercomplex', depending on the complexity of their receptive fields and their requirements for optimal excitation.

'Simple' cells respond best to slits of light or dark on contrasting background or to borders between light and dark regions. To be most effective the slit or border must occur at a particular position in the visual field and must have a particular orientation (horizontal, vertical or oblique).

'Complex' cells also require slits or edges of light or dark at a particular orientation. However, requirements of position are different in that an edge of the correct orientation is effective if it falls anywhere within the receptor field. Many complex cells show a preference for movement of the slit in a particular direction.

'Hypercomplex' cells require an edge not only of precise position and orientation but also of fixed length. Thus, for optimal excitation, the edge must come to an end or change in direction (as in a corner) within the receptive field. 'Hypercomplex' cells have been further subdivided into 'lower' and 'higher' orders depending on their stimulus requirements.

The responses observed in a cortical cell are presumably due to inputs which converge from several lateral geniculate cells, which in turn perceive inputs from ganglion cells whose receptive fields are organized in a linear array. Thus the cells of the visual pathway are organized so as to process information about line, contrast and movement. The types of response described above are found in the striate and peristriate cortex. These cortical areas are obviously concerned with other visual functions besides pattern recognition (i.e. colour vision, binocular vision and movement). The peristriate cortex then projects to other cortical regions such as the inferotemporal cortex. Cells here show a great diversity of responses with large receptive fields (ipsilateral, contralateral and bilateral) and a sensitivity to moving stimuli or to complex visual patterns. Ablation experiments indicate the importance of this area for 'higher' visual functions such as the learning of visual tasks.

Organization of the visual cortex. The cortex is divided anatomically into six layers which lie parallel to the surface. Little is known of the functional differences between the layers. The visual cortex is further organized on a functional basis into columns which lie perpendicular to the surface and extend the full depth of the cortex. Responses of the cells within these columns indicate a further specialization in signal processing. It is now known that there are two independent but overlapping columnar systems. The first of these to be discovered was that of *receptive field orientation.* Thus all cells in one column (approximately 20-50 microm wide) show not only similar receptive fields but also respond to the same orientation of a light slit or dark bar. Cells in an adjacent column have an orientation by only a few degrees so that there is a gradual shift in orientation through the cortex and all orientations are represented.

Superimposed on these orientation columns are *ocular dominance columns* which are wider (500 microm). These columns alternate with each other so that all the cells within one column respond preferentially to inputs from one eye, while those in the adjacent columns respond to the other eye. Normal development of ocular dominance columns requires the normal use of both eyes. Monocular deprivation leads to a reduction in width of the corresponding columns or an associated expansion of those of the functional eye.

Thus an area on the retina of each eye is represented by a corresponding block of cortex (approximately 1-2 mm^2) which contains an ocular dominance column for each eye, with these further subdivided into orientation columns. An adjacent point on the retina is represented by an adjacent block of cortex. There is now evidence that other cortical regions concerned with responses to colour and movements may also have a columnar organization, so that this may be fundamental to the analysis of visual information.

Binocular Vision

The visual fields of the two eyes overlap in the central part to give a region which can be viewed binocularly. The images falling on the two retinae are not identical but neural mechanisms allow them to be interpreted as single images. For this fusion to occur the image of an object must fall on corresponding points of each retina. If such correspondence is prevented in the young child (i.e., by a squint) permanent impairment of fusion can occur.

The neural mechanisms which allow for fusion occur within the cortex. Many cortical cells can be excited by inputs from both eyes. The fields of such binocular cells occur at approximately corresponding points on each eye. However, one difference is in the relative effectiveness of the two eyes. In most cases one eye is more effective than the other, a condition known as *ocular dominance.*

Cells responsive to both eyes are present at birth. Binocular responsiveness of most cells is gradually lost during early life if normal binocular vision is prevented (i.e. by occlusion of one eye or production of a squint). Interestingly, closure of both eyes preserves binocular responses, thus suggesting a competitive effect between activity from the two eyes. Prevention of binocular vision in later life, in both man and animals, is far less likely to lead to failure of fusion. As discusses previously the explanation for these observations appears to lie in the development during early life of the appropriate ocular dominance columns for each eye.

Depth perception. Although most binocular cells require very similar stimulus characteristics for each eye, receptive fields of some cells show slight lack of correspondence known as *receptive field disparity*, which is though to be important in discrimination of depth. However, in man, other clues are also highly relevant. Such clues include the obscuring of parts of objects by others, shadow effects, relative sizes and relative movements.

Colour Sensation

Sensations of colour are due primarily to the presence of three types of cones containing different photopigments and maximally sensitive to different wavelengths of light. Thus there are *red-sensitive cones (peak 565 nanom)*, actually yellow but extends into red,

green-sensitive cones (peak 540 nanom) and *blue-sensitive cones (peak 440 nanom),* and sensations of colour will depend on the extent to which each type is excited. This is termed the *Young-Helmholtz* or *trichromatic theory of colour vision.*

The three cone types do not have separate connections to the central nervous system. Certain horizontal cells and ganglion cells, called *spectrally opponent cells,* show inhibitory interactions between light of different wavelengths. These opponent cells are of four basic types:

(i) excited by red, inhibited by green;

(ii) excited by green, inhibited by red;

(iii) excited by yellow (i.e. presumably connected to both red and green cones), inhibited by blue;

(iv) excited by blue and inhibited by yellow.

The receptive field organization of spectrally opponent cells may be identical over its whole extent (i.e. excited by red and inhibited by green anywhere in the field) or it may show centre-surround antagonism (i.e. excited by red in the centre and inhibited by green in the periphery). Such interactions explain why red and green or yellow and blue are complementary colours. Responses of the opponent cells are also the basis for the after-image of a coloured stimulus appearing as its complementary colour. In primates spectrally opponent cells also occur in the lateral geniculate nuclei and in the primary visual cortex.

Defects in colour vision. Individuals with normal colour vision can match any spectral colour by using a mixture of the three primary colours and are therefore known as *trichromats.* Those who require only two primary colours to match the spectrum are called *dichromats* and those who can match any colour by varying the intensity of only one primary colour are called *monochromats.* Monochromats are totally colour blind and perceive only different shades of grey.

If a trichromat requires more of one primary colour than normal to effect a match he is said to be anomalous and may be classified as *protanomalous* (weak red sensitivity), *deuteranomalous* (weak green sensitivity) or *tritanomalous* (weak blue sensitivity). Dichromats have a more severe colour defect and lack one of the cone pigments. Their colour blindness is distinguished as *protanopia, deuteranopia* or *tritanopia* which literally mean defects of the first (red), second (green) or third (blue) pigment systems respectively. In practice both protanopes and deuteranopes confuse red and green because the spectral absorption curves of their respective green and red pigment system overlap.

5.2 Taste

The sense of taste (gustation) is important in the selection and enjoyment of food, but full appreciation requires tactile, visual and olfactory inputs as well, as is shown by the loss of taste when the nose is blocked.

Gustatory Receptors

These are located in the *taste buds* found mainly on the papillae of the tongue, with a few on the epiglottis, soft palate and pharynx. They are 50 to 70 microm in diameter and open on to the surface of the tongue at the taste pore. Each taste bud is packed with receptor cells (*taste cells*) which are specialized epithelial cells and have nerve endings on their base. Each taste bud also contains some supporting cells. In man there are about 10000 taste buds, the number decreasing with age. Three to five buds are found on each of the *fungiform papillae* at the sides and tip of the tongue while hundreds are found in the grooves of the larger *vallate papillae* at the back. A third type, the *foliate papillae,* are arranged in folds at the back edges of the tongue. Taste cells are constantly shed, with a half-life of approximately 10 days, and are renewed by division of the surrounding epithelial cells. They are also dependent on their nerve supply: denervated taste buds degenerate and reappear again when the nerve regenerates.

Taste receptors are chemoreceptors. Chemicals enter the pore and react with the microvilli on the receptor cells to alter membrane permeability in an unknown way. Classically, four basic tastes are recognized: *bitter, sweet, sour* and *salty*. Some taste buds responds to only one of these, others to more. Cat, dog, pig and monkey also have buds which respond to water. The taste experienced varies with position of the tongue - bitter at back, sweet at tip, sour at edges and salty at tip and sides.

The sensation of sourness is produced by acids and is related to the H+ concentration, but not all acids are equally sour at equivalent pH. Salty sensations are elicited mainly by anions of inorganic salts, particularly chloride, but also by other halides, sulphate and nitrate. Many organic compounds are described as bitter, i.e. quinine, nicotine, morphine and strychnine. Most sweet substances are also organic, i.e. sucrose, maltose, lactose, glucose, saccharine, cyclamate, glycerol, but so too are salts of lead and beryllium. Recently two proteins which are intensely sweet have been discovered.

Afferent Nerves and Central Pathways in Gustation

Taste buds on the anterior two-thirds of the tongue are supplied by the chorda tympani branch of the facial nerve, those on the posterior one-third by the lingual branch of the glossopharyngeal nerve. The vagus nerve supplies taste buds on the epiglottis. Each bud receives branches from many fibres. Taste fibres join in the medulla to form the tractus solitarius and synapse first in the nucleus solitarius. The second order fibres cross the midline and run in the medial lemniscus to the most medial part of the ventroposterior medial nucleus of the thalamus. The cortical projection goes to the face region of the somatosensory cortex.

5.3 Smell

In many animals the sense of smell (olfaction) is important for the selection of food, in sexual activities and in the recognition of other animals and of territories.

Olfactory Receptors

The receptors lie in the specialized olfactory epithelium lining the roof of the nasal cavity, and cover an area of about 5 cm^2 in man but relatively much more in such animals as the dog. The epithelium contains supporting cells which secrete mucus and receptor cells (*olfactory cells*) which are specialized *bipolar neurones*. The apical region of these bipolar neurones end in cilia which are embedded in mucus. The basal end gives rise to a fine (0.2 microm) unmyelinated axon which passes to the olfactory bulb. These receptor cells are the only nerve cells in adult mammals which show continual degeneration. They are replaced by division and differentiation of other neuroepithelial stem cells.

Several thousand chemicals can be smelled. To be detected they must reach the olfactory epithelium by diffusion which can be aided by sniffing to increase the air flow. The chemicals are mainly organic, containing three to twenty carbon atoms, but there is no simple relationship between chemical structure and odour. They must be volatile and have some water solubility in order to dissolve in the mucus and also have lipid solubility to interact with the receptor membrane. Threshold concentrations vary, being extremely low for certain substances i.e. 0.4 nanog/L air for methyl mercaptan (garlic). The stimuli presumably react with receptors in the membrane to cause a permeability change. Chemical stimulation gives rise to a mass response recorded as a potential difference across the olfactory epithelium, called the *electroolfactogram*, which is a monophasic negative potential.

The sense of smell shows very marked adaptation and is subject to 'masking' of one smell by another - the basis for 'air fresheners'. Olfactory acuity is also better in women than in men, particularly at the time of ovulation, and has been positively related to oestrogen levels.

Afferent Nerves and Central Pathways in Olfaction

The unmyelinated axons of the receptor cells pass through the cribriform plate and enter the olfactory bulb to end in a glomerulus, where they make their first synapse with mitral and tufted cells. From here, second order axons travel to the opposite olfactory bulb and project in the olfactory tract to various regions of the limbic system (anterior perforated substance, septal nuclei, amygdala and prepiriform cortex and hypothalamus). Some reports also suggest connections to the mediodorsal nucleus of the thalamus and hence to the neocortex.

5.4 Hearing

The sensation of sound detected by the ear is caused by variation in air pressure within a specified range of frequencies and intensities. Outside this range the sensations evoked are variously described as vibration, flutter, tickle and pain.

A source of sound such as a tuning fork causes the surrounding air molecules to oscillate. The disturbance spreads out from the source in sinusoidal waves which consist of areas of compression of air (high pressure) alternating with areas of rarefaction (low pressure). The *loudness* of the sound is related to the amplitude (pressure difference) of the sound wave and the *pitch* to the frequency. A *pure tone* is a sound of only one frequency.

Aspects of a Sound Stimulus

Frequency. The range of frequencies of sine-waveform, commonly called sound, extends from about 20 to 20000 Hz, nearly ten octaves of pitch range. Higher frequencies are called ultrasound and lower, infrasound, which in some people causes sensations of malaise and oppression. Frequency discrimination is best around 1 kHz where it is about 0.3% of that frequency (or 1/22 semitone), falling to 0.5% at 10 Hz and 3.0% at 100 Hz (about 2/3 semitone), giving a total of 1600 discriminable pitches, i.e. steps of subjective highness or lowness of notes.

Almost all sounds are complex, rather than simple, sine-waves and their waveforms can be split by Fourier analysis into a number of component sine-waves, all harmonically related, i.e. the higher ones have two, three and more times the frequency of the lowest one present. The lowest is the 'fundamental' and the others are 'second', 'third' and so on, 'harmonics' or 'upper partials'. The number and intensity of each determine the tone or timbre of the sound, whilst the fundamental determines the pitch. Thus the range and strength of the violin's upper partials are greater than for the tube and give the violin a brighter tone.

Intensity. This is the objective aspect of a sound stimulus, measurable with instruments, whilst 'loudness' is the subjective, conscious aspect, which is harder to quantify. The intensity of sound is the amount of energy passing through a unit area per unit time and is given in W/m^2. The threshold of hearing varies with the stimulus frequency and is least over a middle range from about 1 to 3 kHz where it is about 10^{-11} W/m^2 in man. The resulting displacement of the tympanum is about the diameter of a hydrogen atom. The threshold rises to 10^6 times this value at 50 Hz and 10^3 times at 10 kHz. Threshold for pain is at 10^{12} to 10^{13} times.

To cover this range of intensities it is convenient to use a logarithmic scale of sound intensities relative to a fixed reference value. The unit of this ratio is the *bel* (named after Alexander Graham Bell) or more often the *decibel (dB).* Thus the intensity in dB of a sound of power y_2 in relation to a reference y_1 is $\log_{10} y_2/y_1$ where y_1, the reference power, is an arbitrarily chosen value which is near the minimum threshold of hearing unless otherwise specified. Intensity discrimination is about 1 dM under the most favourable experimental conditions, but more usually 2-3 dB, i.e. nearly double the sound power, so that at 1-3 kHz there would be no more than about 130 steps of loudness from threshold of hearing to threshold of pain.

Duration. To establish a pitch requires a minimum duration of 15 to 20 msec which surprisingly enough hardly varies with frequency.

Direction of sound source. Discrimination of the direction of the sound source is best at frequencies above 1 kHz and depends on (i) intensity differences at the two ears resulting from the shielding effect of the head, and (ii) differences in time of arrival of the wavefront at the two ears which is never greater than about 1 msec and can be detected when as little as 30 microsec.

Functional Anatomy of the Ear

The ear is divided into outer, middle and inner ear compartments.

Outer ear. The *external auditory meatus,* about 27 mm long, conducts air pressure variations from the *auricle,* pinna or ear flap to the *tympanum* or ear-drum. The air column has a resonant frequency of about 3 to 4 kHz and conducts energy to the ear-drum most effectively in this range.

Middle ear. The outer ear and the middle ear are separated by the ear-drum or tympanum. The cavity of the middle ear is connected to the pharynx by a narrow passage called the *Eustachian tube* which allows the pressure of the air in the middle ear to equilibrate with the outside pressure. Connected to the tympanum is the *ossicle chain* of *malleus* (hammer), *incus* (anvil) and *stapes* (stirrup) which is set into and almost fills the *oval window* between the middle and inner ear. The ossicle chain, together with the smaller area of the oval window relative to the tympanum, operates to promote the efficient transfer of energy from air to the liquid environment of the inner ear, i.e. it acts as an impedance matching device. The resonant frequencies of the middle ear mechanism are around 800-1200 Hz and, with the broadly tuned resonance of the external auditory meatus, are mostly responsible for the low threshold of hearing in this frequency range.

The effectiveness of the ossicle chain can be modified by the activity of the middle ear muscles. The *tensor tympani muscle* pulls the tympanum inwards and this results in the stapes being pushed into the oval window. The *stapedius muscle* pulls the stapes out of the oval window and pushes the tympanum outwards. When they contract together, they stiffen the middle ear mechanism to reduce the transfer of energy into the inner ear. They do so in response to high intensity sounds, with a latency of about 10 msec, but soon relax again during constant stimulation.

Inner ear. This has a bony coiled tube of two and a half turns, the *cochlea,* divided by membranes along its length into three parallel canals or scalae, called the *scala vestibuli,* the *scala media* or *cochlear duct* and the *scala tympani*. The scala vestibuli and scala tympani are filled with *perilymph* and join at the *helicotrema.* The cochlear duct is filled with *endolymph.* The cochlear duct is separated from the upper scala vestibuli by *Reissner's membrane* and from the lower scala tympani by the *basilar membrane.* When the stapes is pushed into the oval window, a wave is conducted along the scala vestibuli, the basilar membrane is depressed and the membrane of the *round window* bulges out into the middle ear.

The basilar membrane is a fibrous structure with fibres running from the inner core or *modiolus* to the outer side of the bony tube, of lengths and thicknesses graded from 0.04 mm long at the 'window' end or base of the cochlea to 0.5 mm long at the apex or helicotrema. The resemblance to the strings of a piano gave Helmholtz (1821-1894) the idea of this resonance theory of pitch discrimination, which has since been modified. Short fibres were supposed to resonate to high frequencies and long ones to low and the receptors standing on these fibres would be stimulated by movement. Thus pitch would be represented by which afferent fibres were active and intensity by the frequency of impulses in them.

The sound receptors of the ear are found in the *organ of Corti* which lies on the basilar membrane within the cochlear duct. It is composed of an epithelium of *hair cells* (Corti cells) and supporting cells. The hair cells are arranged into inner and outer groups. Each hair cell is anchored on the basilar membrane and has a hair bundle projecting from its tip through the stiff and impervious *reticular lamina* to be embedded in the shelf-like *tectorial membrane.* Afferent fibres of the cranial nerve VIII or auditory nerve arborize around the hair cells and converge into the bony modiolus or core of the cochlea.

When the basilar membrane moves up and down it tends to move rather rigidly, bending about an axis near the modiolus. The tectorial membrane is pushed up and pulled down and there is a shearing motion between the tectorial membrane and the reticular lamina bending the hairs to one side and the other.

In order to get a fuller picture it is necessary to consider not only radial movements of the basilar membrane, but also how movements along its length from base to apex are determined by the frequency of the sound. When it became possible to observe this directly, Helmholz's speculations had to be modified. In experiments dating from about 1930, G. von Bekesy examined the moving basilar membranes of many animals, from mouse to elephant, and showed that the pattern of movement during steady sine-wave stimulation conformed to what is termed a 'travelling wave', whose progress, like that of an arterial pulse, shows an instantaneous amplitude and velocity which can change all along the tube depending on the elasticity of the tube wall, and the energy absorption from the wave up to any point.

In the diagram are shown the displacement caused by a 200 Hz wave instantaneously (solid line) and the envelope of all displacements over a period of many cycles (dashed line). It can be seen that (i) the velocity of propagation is diminished over the last part of travel, (ii) there is a region of maximum displacement quite far from the oval window, (iii) all the basilar membrane from the oval window up to this point moves to a lesser degree, (iv) the amplitude falls off quickly beyond the maximum, and (v) at any instant some parts of the membrane are displaced upwards, others downwards.

Inevitably, the receptor discharge in response to the progress of this wave must be very complex. The peak displacement position of the basilar membrane is closer to the stapes the higher the frequency.

Mechanism of Stimulation of the Cochlear Afferent Fibres

The endolymph in the cochlear duct (scala media), which is continuously secreted by a plexus of blood vessels called the *stria vascularis,* is very close to ICF (intracellular fluid) in composition. Because of the impervious nature of the reticular lamina through which the hairs of the Corti cells protrude, only these hairs are surrounded by endolymph, and the larger remainder of the Corti cell membrane is surrounded by perilymph, which fills the scala tympani and scala vestibuli and is close to cerebrospinal fluid and ECF (extracellular fluid) in composition.

The stria vascularis generates a secretory potential of about + 80 mV in endolymph relative to perilymph. It has been postulated that the effect of bending the Corti cell hair in one direction is to reduce the resistance of the reticular lamina and allow current to be driven

by this 'endocochlear potential' of 80 mV through the Corti cell into adjoining tissue. This results in excitation of fibres of cranial nerve VIII and thus determines the frequency of action potential generation. If it turns out that excitation of the afferent fibres is by chemical transmitter liberated by the Corti cell, this hypothesis will still serve, since the quantity of transmitter liberated would be determined by the current through the Corti cell membrane.

There is a small tract of efferent fibres ending on or close to the Corti cells, the olivocochlear bundle, which has an inhibitory action, reducing the afferent discharge at a given stimulus intensity. Its employment by the CNS is not well understood.

Action Potential Discharges in the Auditory Nerve

We shall now look for correlations in the discharge pattern between basilar membrane deflections as determined by travelling waves and features signalling the frequency and intensity of the sound stimulus.

Many single afferent fibres are spontaneously active in the absence of a stimulus. At sine-wave stimulus frequencies up to 1 kHz, the firing of single fibres can 'follow' the sine-wave in the sense of occurring only in corresponding halves of successive cycles. Since nerve fibres cannot carry more than about 1000 action potentials per second, when stimulus frequency is increased beyond this a fibre which had previously given one spike in each cycle will begin to drop out once every few cycles and so on. At these higher stimulus frequencies a *group* of fibres, missing fire in an independently assorted fashion, can give discharges which when recorded from the group rather than from a single fibre can keep in step up to about 3 kHz. Thus fibre A would respond to cycles 1, 4, 7 and so on, fibre b to cycles 2, 5, 8, and fibre C 3, 6, 9. Above 3 kHz no clear visible relation can be made out in the discharge of a single fibre to the stimulus waveform.

If the stimulus thresholds are determined for a single fibre at various frequencies and intensities, it is found that they rise rapidly on both sides of one small range of frequencies (the 'best' frequency) but more steeply on the higher frequency side, so that usually some high frequencies cannot provoke discharge, however intense they are. Note that as the stimulus intensity is raised the fibre responds over a wider frequency range. A little reflection will show why the shape of the 'response area' for this fibre above the dashed line fits well with the envelope of displacement to the basilar membrane caused by travelling waves of various frequencies acting on a receptor situated at a point along the basilar membrane.

We are now in a position to describe how the auditory information is encoded in auditory nerve fibre discharges with reference to the four properties of a sound stimulus discusses earlier.

1. *Pitch* discrimination is mainly determined by the area of basilar membrane occupied by firing receptors for a given stimulus frequency (the 'space' principle). High notes stimulate receptors closed to the base of the basilar membrane and low notes stimulate receptors closer to the apex. In addition, it has been argued that the pattern of periodicity of action potentials in the auditory nerve may provide information about the pitch of a sound at low frequencies (the 'periodicity' principle).

2. *Intensity* sensation is derived from the total number of impulses per second in the auditory nerve fibres. At a given stimulus frequency only certain fibres will respond to a low intensity stimulus. As the stimulus intensity is raised the discharge frequency in these firing fibres is increased and previously silent fibres with higher thresholds at that stimulus frequency are recruited.

3. *Duration of stimulus* is signalled by the total duration of the afferent spike discharge caused by the stimulus.

4. *Direction of the sound source* is signalled by preservation in the auditory pathway of (part of) the initial time difference in receptor activation on the two sides of the head, as well as continuing intensity differences.

This information is now delivered to the medulla and processed at each synaptic relay in the path to cerebral cortex and elsewhere, and of course at the destination.

The Central Auditory Pathways

The auditory pathway from the Corti cell to the thalamus is a polysynaptic chain of at least four neurones. Some impulses travelling along this pathway may be side-tracked to re-enter the direct path by longer chains. The main synaptic regions are in the dorsal and ventral cochlear nuclei and the olivary complex (all in the medulla), in the nucleus of the lateral lemniscus, in the inferior colliculus and in the cerebral cortex. The main cortical area is deep in the lateral or Sylvian fissure, emerging at the surface near the middle of the dorsal border of the superior temporal gyrus. Both ears are represented in both right and left cortices. Collateral branches from the pathway travel to spinal levels, the cerebellum and reticular formation of the brain-stem and to the superior colliculi.

There are also inhibitory endings derived from higher levels of the CNS at each afferent synaptic level so that some modification of the afferent discharge must occur in these integrating centres.

Deafness

Hearing impairment in the sense of a raised threshold to sound stimuli may be due to impaired sound transmission in the outer or middle ear (conduction deafness) or to damage to the receptors or to the neural pathways (sensorineural deafness).

Conduction deafness may be caused by:

1. Narrowing or blockage of the external meatus as by pus, wax, coal-dust etc.

2. Thickening of the tympanum following scarring or repeated middle ear infections.

3. Exudate in the middle ear (otitis media).

4. Dislocation or fixation (ankylosis) of the ossicle chain.

5. Otosclerosis, which is a narrowing of the gap between the footplate of the stapes and the surrounding bone, progressing to fixation of the footplate when the gap is bridged.

Sensorineural deafness caused by damage to the organ of Corti results from high intensity stimulation of long duration, predominantly of high frequencies, as in such trades as boilermaking. Ear protection is considered desirable where the ambient noise level is more than 85 dB above threshold in the range 300-2400 Hz. Other sorts of nerve deafness can be caused by some antibiotic (streptomycin), by mechanical damage to CN VIII, by a tumour, or by diseases such as meningitis, rheumatism, malaria and syphilis.

5.5 Vestibular Function

The vestibular system provides information on the spatial orientation of the head and is therefore essential in posture and movement. The simplest definition of the vestibular apparatus seems to be 'the non-auditory part of the inner ear'.

Anatomy of the Vestibular Apparatus

The vestibular apparatus consists of the *semicircular canals,* the *utricle* and the *saccule,* together with auxiliary structures. It is a *membranous labyrinth* composed of a series of tubes filled with endolymph and surrounded by perilymph, which in turn is contained in a bony cavity of the same shape as the membranous labyrinth and called the *bony labyrinth.*

The three semicircular canals lie in nearly orthogonal planes, each is at right angles to the other two. When the head is held erect the truly lateral or so-called horizontal canal is raised anteriorly at about 30° to the horizontal; the superior (anterior) and posterior canals are at 45-55° to the sagittal and frontal planes respectively. The two lateral canals, on the right and left side of the body, are in a single plane and the posterior canal of one side is in a plane nearly parallel to that of the anterior canal of the other side, which causes the two to be stimulated similarly. The canals of either side alone can generate afferent impulses signalling movement in any direction and from this point of view only one labyrinth is essential.

Each canal is connected at both ends to the utricle and has at one end an enlargement, the *ampulla,* containing receptors transducing motion into nervous impulses. The receptor apparatus, called the *crista ampullaris,* consists of the *cupola* (or cupula), a gelatinous wedge-shaped structure running fully across the cross-section of the ampulla, and, at least in man, apparently preventing fluid motion past it. It has very nearly the same specific gravity as the endolymph, and hence, whatever the position of the head, it neither floats upwards nor sinks down and thus is nearly incapable of registering the direction of gravity. Into the thick end of this wedge projects a ridge carrying many hair cells whose processes are embedded in the gelatinous cupola.

Both the utricle and the saccule have a patch or *macula* of hair cells also projecting into and embedded in a gelatinous mass. This however also contains above the hairs an *otolith* composed of a mass of calcium carbonate crystals called *otoconia*.

Each hair cell has a bundle of sixty to a hundred filaments forming the hair. All but one are hexagonally packed and of progressively increasing length towards one side of the bundle and are called *stereocilia.* A specially long filament, the *kinocilium,* which is of different structure, stands out at one side. Movement of endolymph towards the side on which the kinocilium stands causes the hair cells to discharge more frequently, and when it occurs in the opposite direction the discharge decreases.

Functions of the Vestibular System

The vestibular system is affected by linear and rotational movements of the head. Classically it is said that the semicircular canals respond to angular accelerations and the otolith organs of the utricle and saccule, also known as gravireceptors and as statolith organs, respond to the direction of gravity force and to linear acceleration. The functions of the vestibular system can be summarized as follows:

1. It contributes to the sensation of motion and of spatial orientation of the head.

2. During head movements it helps to maintain a stable image on the retina by causing compensatory eye movements.

3. It contributes to the maintenance of balance, i.e. to equilibration, in various postures, by altering the distribution of tone in various muscle groups.

Vestibular signals are combines with visual and other proprioceptive, exteroceptive and sometimes auditory information in conscious spatial orientation and the mostly subconscious maintenance of equilibrium

Stimulation of the Vestibular Afferent Fibres

Deflection of the cupola causes bending of the hairs and this occurs whenever endolymph moves along the canal. Since the fluid must have a source on one side of the cupola and a destination on the other side, the connections to the utricle are essential. The flow is soon stopped by the deflection of the cupola which generates elastic tension equal to the fluid pressure producing it. The maximum pressures occur at times of *change* in angular velocity of the head since they are caused by the inertial tendency of endolymph to remain in a constant position, usually relative to the earth. During steady motion, friction between the fluid and the walls of the semicircular canal will accelerate the fluid until its velocity reaches zero with relation to the walls. At this stage, the cupola returns slowly back to its resting position and the fluid is redistributed.

There is a spontaneous tonic discharge of the receptor hair cells which is changed when the hairs are bent. In the figure is shown the change in impulse frequency in afferent fibres when the head is rotated to the right at a constant speed. After an initial increase in frequency the discharge returns to its frequency at rest and the sensation of movement ceases. This takes about 25 to 30 sec in man. When rotation is stopped quickly the opposite sequence takes place. The discharge frequency of the receptors changes in the opposite direction to that of the beginning of rotation and there is a feeling of moving in the opposite direction until the fluid has been slowed to a stop.

The discharge patterns from the ampullae of corresponding semicircular canals on the two sides of the body are mirror images, but either canal signals the whole pattern. No additional information is made available by the other canal, so presumably this reduplication serves as a safety device.

In the otolith organs of the utricle and saccule the specific gravity of the otoconia is approximately 2.9, much higher than that of the endolymph. The otolith consequently tends to fall to the lowest possible point. It follows that its equilibrium position will be determined by the direction of the force of gravity. Also, by having a different inertial mass from that of an equal volume of endolymph, the otolith will tend to move in relation to the macula in response to all accelerations of the head, linear or rotational.

Action Potential Discharges in Vestibular Fibres

In experimental animals spontaneous rates of firing in different vestibular fibres vary from a few per second up to about 200 per second, averaging 90. The frequency of this discharge is altered by bending the hairs of the hair cells.

To a first approximation the ampullae of the semicircular canals are sensitive to angular acceleration and the maculae of the utricle and saccule to the direction of gravity and to linear acceleration. However, they can all respond to other modes of stimulation to some extent. In the crista ampullaris each and every hair cell has its kinocilium at the corresponding side of the cell. For the ampulla of the lateral canal all the hairs are oriented with their kinocilia towards the utricle, but in the other canals the kinocilia are towards the canal and so movement of fluid towards the utricle stimulates the hair cells of the lateral canals, but inhibits those of the vertical canals. In the macula things are more complex and the hair cells do not have the same orientation with respect to the position of their kinocilia. There is a line of reversal in the orientation of the hair cells in the maculae of the utricle and saccule. Unlike the hair cells in the macula of the utricle those in the macula of the saccule have their kinocilia oriented away from each other rather than toward each other on either side of the line of reversal. As a consequence of these complex patterns of orientation of the hair cells each different movement of the otolith causes a different spatially organized pattern of discharge in the afferent fibres. These highly organized afferent patterns generated in different parts of the system probably account for the direction of the compensatory eye movement which occur.

There is a small tract of efferent fibres to the vestibular apparatus whose function is probably inhibitory as for the corresponding supply to the cochlea. These efferent fibres may play a role in *habituation* to repeated patterns of acceleration, of which one subjective example is 'getting your sea-legs' on boats. This is partly a peripheral phenomenon, that is, the afferent discharge in a given vestibular fibre falls off with repetition of the movement which causes it, and this may be due to inhibition of the receptor discharge by efferent fibres.

How do the discharges described above assist in the three functions mentioned at the outset: sensation of motion and gravity, maintenance of a stable retinal image and contribution to equilibrium?

1. Sensation of position and movement of the head may reasonably be supposed to involve some parts of the cerebral cortex, which in this cases are close to the main auditory sensory area which is in the temporal lobe, tucked into the lateral or Sylvian fissure.

2. In maintaining a stable retinal image during head movements by causing compensating eye movements, two quite different reflexes are involved. For all head movements which occur whilst an object is being looked at and for movements of the object itself, there exists a *fixation reflex* which by pursuit movements of the eye keeps the image of the object on the part of the retina giving the clearest vision, the fovea centralis. This reflex obviously involves some highly complex manipulation of afferent information to detect the sharpest vision and involves participation of the visual parts of the cerebral cortex. There is a limit to the amount by which an eye can be turned in the head to follow an object and when it is reached either head movement must occur or the eye can quickly return to roughly the straight ahead position, find another object of interest and follow it. This latter process happens when one watches the world go by from a moving vehicle and is called *optokinetic nystagmus.* The word 'nystagmus' refers to any oscillatory movements of the eyes whether normal or pathological and especially to this slow turn, quick return sequence just described. The direction of the nystagmus is conventionally named according to the quick phase.

The other mechanisms by which the eyes are moved so as to keep an image as far as possible steady on the retina is driven by the vestibule and takes place to some extent whenever the head is moved, even in total darkness. It is driven by the rotation receptors and is called *vestibular nystagmus.* Here the slow drift is in the opposite direction to the rotation of the head and the quick phase is in the same direction. In the dark this reflex is only about 60% effective in the sense that drift of the eyes is about 60% of the rate of the rotation of the head. In the light, this reflex collaborates with the fixation reflex. Connection between the vestibular nuclei and the motor neurones of the extrinsic ocular muscles is by the medial longitudinal bundle.

3. The third function of the vestibule is the maintenance of balance, that is, equilibration in various postures by determining the distribution of tone in different muscle groups, in other words, participation in postural activity, for which the connections of the vestibular nuclei of the medulla with spiral motoneurones by the vestibulospinal tract and with the cerebellum are evidently important.

Disorders of Vestibular Function

Semicircular canal function can be tested by rotating the subject in a special chair whilst the head is held in such a posture as to stimulate one functionally-associated pair of canals selectively. One can examinee the consequences of stopping rotation on either eye movements or on body muscle tone. The latter is manifested by a tendency to deviate from a straight line when walking with the eyes closed. In these procedures both right and left canals are inevitably stimulated together.

Unilateral stimulation can be produced by running water at above or below body temperature into the external meatus of the ear - the *caloric test.* The temperature difference gives rise to convection currents in the endolymph which excite the hair cells. This produces nystagmus which can be compared with a known normal response.

Diseases affecting the vestibule or its afferent fibres can cause abnormal discharges producing a sensation of *vertigo*, or giddiness, in which the external world may seem to move, the body may be felt to be moving, or the posture of the limbs, especially the legs, may be felt to be unsteady. Along with this there may be nystagmus, double vision, actual falling, and autonomic signs such as pallor, sweating, pulse rate and blood pressure changes, nausea and vomiting. *Meniere's disease* is characterized by attacks of vertigo and progressive impairment of hearing. The cause is unknown but on post-mortem examination the endolymph-filled chambers of the inner ear are found to be enlarged.

When an often-repeated cyclical pattern of strong stimulation of the labyrinth occurs, as in sea travel or land travel in a car along a winding road, similar physiological consequences occur and are known generally as *motion sickness.*