Transient positional nystagmus has been repeatedly observed following the ingestion of water- and lipidsoluble molecules with specific gravities differing from that of endolymph, such as alcohol or “heavy water”. The semicircular canals selectively transduce angular velocity and head acceleration, and under normal circumstances are insensitive to gravitational orientation and linear acceleration. A major reason for this insensitivity to head orientation in space is that the cupula and endolymph have the same specific gravity of 1.0087 relative to water (the sensory hair cells are embedded in the cupula which is housed in the ampulla of the canals). The neutral buoyancy of the cupula in the endolymph prevents any out-of-balance forces when linear accelerations are applied.

If there is a considerable specific gravity differential between cupula and endolymph, the semicircular canals will become sensitive to changes in head position within the gravitational field, resulting in positional rotatory vertigo and nystagmus. The direction of both nystagmus and vertigo should be dependent on

1. the particular head position (according to the different planes of the horizontal and vertical semicircular canals) and
2. on whether the specific gravity of the cupula is greater or less than that of the endolymph.

Thus, nystagmus should change direction with either head position right lateral or left lateral and beat

1. toward the undermost ear when the cupula is “lighter” than endolymph or
2. toward the uppermost ear when the cupula is “heavier” than endolymph.

This hypothesis – also called the buoyancy hypothesis – requires that ingested water-soluble compounds of different specific gravity diffuse at different speeds into cupula and endolymph, thus causing a transient density gradient. Experiments conducted with ethanol, deuterium oxide, and glycerol induced positional nystagmus, which is consistent with the hypothesis.

The pathophysiological concept of a gravity differential between cupula and endolymph, which causes a positional vertigo/nystagmus (alcohol, glycerol, heavy water, macroglobulinaemia), leaves several questions open (Brandt 1990). For example, why is positional alcohol nystagmus maintained for minutes to hours in the precipitating head position? Is it because the gravity-dependent deflection force is greater than the physiological restoring force? This explanation is consistent with a constant deflection of the cupula, which would provide continuous mechanical stimulation of the hair cells. The gravitational force would be balanced by the elastic restoring force of the cupula tissue at some deflected position (Fig. 17.1). The normal time constant (7 s time constant of the cupula; cupulogram) seems to result from the endolymph viscosity opposing the elastic restoring force that is intrinsic to the cupula when the stimulus is removed. However, it seems strange that the hair cells fail to adapt, which is implied by this long-lasting response.

The common view that benign paroxysmal positioning vertigo (see BPPV, p. 257) is induced by the same mechanism (Schuknecht 1969; Rietz et al. 1987) cannot be correct, however, for several reasons. First, BPPV is a positioning rather than positional vertigo/nystagmus, because it is induced only by rapid changes in head position. Second, BPPV subsides after 10–60 s and ultimately abates even when the precipitating position is maintained. Third, symptoms of vertical and horizontal canal BPPV are compatible with a free-floating clot (canalolithiasis, see Chap. 16, p. 259) rather than a “heavy cupula” (cupulolithiasis).

If the concept of cupulolithiasis, “heavy cupula,” is valid, two findings remain unclear. Why do patients with BPPV not suffer from additional positional vertigo/nystagmus? Why do compounds with differing specific weights (such as alcohol and “heavy
water”) induce positional but not positioning nystagmus with rapid changes in head position? If they do, then for alcohol this positioning nystagmus should beat toward the same direction as positional nystagmus during the resorption phase (PAN I, when the cupula is relatively lighter) but toward the opposite direction during the reduction phase (PAN II, when the cupula is relatively heavier).

There is little mention of possible effects of the various molecules on endolymph viscosity, neural activity, and adaptation (Zucca et al. 1995; Takumida et al. 1995), and one may wonder if this has any relevance to the difficulty of reconciling theory and clinical findings? Depending on the diameter of the semicircular canal, lower endolymph viscosity should produce a faster response (tending to sense acceleration rather than velocity) and a shorter time constant of the system. Higher viscosities should lead to reduced gain and a longer time constant for decay of the output, unless the adaptation of the sensory cells to a constant stimulus has a significant effect. Further experiments are needed to clarify these discrepancies between theory and clinical manifestation. As fascinating as positional nystagmus and vertigo are, if they are caused by the buoyancy mechanism, the clinical relevance of the four conditions is minimal:

• positional alcohol vertigo/nystagmus (PAN)
• positional “heavy water” nystagmus
• positional glycerol nystagmus
• positional nystagmus with macroglobulinaemia

In the differential diagnosis of positional nystagmus (p. 247), it is helpful for the clinician to know that in outpatients, who present after alcohol excess the night before, PAN beats toward the uppermost ear (alcohol reduction phase, p. 287). The same is true for the rare positional nystagmus and vertigo secondary to macroglobulinaemia.

**Positional alcohol vertigo/nystagmus (PAN)**

Bárány (1911) described the direction-changing characteristics of positional alcohol nystagmus in humans with changes in head positions (beating toward the undermost ear). This was later proven in animals (Rothfeld 1913; De Kleyn and Versteegh 1930; Goldberg and Störtebecker 1941). The reversal of direction in PAN (beating toward the uppermost ear) hours after alcohol intake was first observed by Walter (1954) and later termed PAN II by Aschan et al. (1956), Aschan (1958) and Money et al. (1965, 1974) in their studies. A peripheral labyrinthine origin of PAN was suggested by observations that it does not occur when labyrinthine function is lost in humans (Harris et al. 1962) and animals (Nito et al. 1964).

Alcohol is lighter than endolymph, and when blood levels approach 40 mg/dl⁻¹, alcohol diffuses into the cupula, rendering it lighter than endolymph and thereby transforming the semicircular canals into gravity-sensitive receptors (Money et al. 1974). Nystagmus and vertigo then occur when the subject lies down. In phase I of PAN, the nystagmus beats toward the undermost ear (Fig. 17.1). With time, blood alcohol diffuses into the endolymph, equalis-

![Fig. 17.1. Ingestion of water-soluble molecules with differing specific gravities, such as alcohol, heavy water or glycerol, causes a specific gravity differential between cupula and endolymph (buoyancy hypothesis) with positional nystagmus and vertigo. During the resorption phase of alcohol, nystagmus beats toward the undermost ear (PAN I with the cupula relatively lighter than endolymph). Positional nystagmus beats toward the uppermost ear during alcohol-reduction phase (PAN II) as well as in glycerol-, heavy water- and macroglobulinaemia-induced positional nystagmus (with the cupula relatively heavier than endolymph). The gravity-dependent deflection force on the cupula (inset, B) must be greater than the physiological restoring force (inset, C) for the positional nystagmus to last as long as the precipitating head position is maintained. (From Brandt 1990.)](https://example.com/fig171.png)