Epidemiology of Paroxysmal Positioning Vertigo: Correlation with Seasons, Climate, and Pollution

Paolo Mariani,[1] Matteo Pelagatti,[1] Ales Hahn,[2] and Dario Alpini[3]

[1] *Department of Statistics, Milano Bicocca University, Milan, Italy;* [2] *Ear, Nose, and Throat Institute, III Medical Faculty, Charles University Prague, Czech Republic; and* [3] *Otoneurology Service Sc. Institute, S. Maria Nascente, don C. Gnocchi Foundation, Milan, Italy*

Abstract: The aim of this article was to evaluate the time course of paroxysmal positioning vertigo (PPV) and to investigate correlations with environmental and seasonal factors through a retrospective statistical analysis spanning 4 years (2001–2004). Applying rigorous diagnostic criteria, we selected 575 patients (429 women and 146 men; age range, 17–94 years; mean age, 55 years for men and 56 years for women). Statistical analysis included events per month and per year. We conducted a descriptive statistical analysis to investigate the correlation between vertigo events and main environmental factors: air pollution as expressed by daily concentration of nitric monoxide and ultrafine particles; air pressure; mean temperature and sun radiation; and humidity. We referred the environmental data, collected by Regione Lombardia (the regional government of Lombardy), to the greater Milan homogeneous area. We performed an analysis of variance test and observed that PPV is more frequent in middle-aged women (in or around their fifties) and on the right side. PPV is clearly negatively correlated with temperature, and frequency of attacks depends on temperature variations. The role of air pollution, especially particles, is suspected, but it is not yet clearly identified. Factors that link climate and otoconia metabolism require further investigation.

Key Words: climate; environment; epidemiology; paroxysmal positional vertigo; pollution; seasonality

Paroxysmal positioning vertigo (PPV) is a major cause of vertigo, accounting for 14% of all equilibrium disorders and an annual incidence of about 100 per 100,000 population [1]. It starts suddenly and is usually first noticed in bed on awakening from sleep. Any turn of the head seems to bring on violent but brief bursts of dizziness. Patients often describe the occurrence of vertigo with tilting of the head, looking up or down, or rolling over in bed. It is not unusual for nausea and vomiting to accompany the vertigo. Even if a spell is brief, a feeling of queasiness may last several minutes or even hours, and those who experience this kind of vertigo are distressed and incapacitated for several days, which has a severe impact on social costs owing to lost workdays. PPV is a common vestibular disorder leading to significant morbidity, psychosocial impact, and medical costs. PPV accounted for 8% of individuals with moderate or severe dizziness and vertigo. The lifetime prevalence of PPV was 2.4%, the 1-year prevalence was 1.6%, and the 1-year incidence was 0.6%. The median duration of an episode was 2 weeks. In 86% of affected individuals, PPV led to medical consultation, interruption of daily activities, or sick leave [1].

Although some aspects, such as life events [2] or lifestyle [3], have been investigated, researchers have not posited any epidemiological correlation between PPV and such environmental factors as climate and pollution. The aim of this research is to evaluate the time course of PPV and to investigate correlations with environmental

Reprint requests: Paolo Mariani, Statistics Department, Bicocca Milan University, via Bicocca degli Arcimboldi 8, 20126, Milan, Italy; Phone: +39-02-64485822; E-mail: paolo.mariani@unimib.it; and Dario Alpini, Ear, Nose, and Throat Institute, Otoneurology Service Sc. Institute, S. Maria Nascente, via Capecelatro 66, 20148, Milan, Italy; Phone: +39-02-40308-322; E-mail: dalpini@dongnocchi.it

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and seasonal factors through a retrospective statistical analysis spanning 4 years.

PATIENTS AND METHODS

We performed a retrospective evaluation of the 2000–2004 database from the Santa Maria Nascente, don Carlo Gnocchi Foundation's Otoneurology Service. The same operator (DA) observed all the patients, and widely accepted, standard criteria to define PPV [4] were adopted, including typical case history, typical nystagmus findings, posturography and, when it occurred, electronystagmography and magnetic resonance imaging. Furthermore, an expert but independent otolaryngologist (AH) examined clinical findings regarding patients affected with positional vertigo to identify only those patients affected with idiopathic PPV (i.e., PPV not related to any known cause). We excluded from the study any patient with traumatic, neurological, or other concomitant vestibular disorder (e.g., vestibular neuritis).

Finally, we considered only patients residing in Milan or its environs to guarantee homogeneous exposure to such environmental factors as pollution and air pressure. In this way, we selected 575 patients (429 women and 146 men; age range, 17–94 years; mean age, 55 years for men and 56 years for women).

Statistical analysis included events per month and per year. We conducted a descriptive statistical analysis [5] to investigate the correlation between vertigo events and main environmental factors:

- Air pollution as expressed by daily concentration of nitric monoxide and ultrafine particles
- Air pressure
- Mean temperature and sun radiation
- Humidity

Environmental data were referred to the greater Milan homogeneous area and were collected by Regione Lombardia (the regional government of Lombardy) [6]. Additionally, we performed a descriptive statistical analysis and an analysis of variance (ANOVA) test.

RESULTS

In our patient pool, 74% of patients were female. Mean age was 56 years in men and 55 years in women. We observed right-sided PPV in 377 patients (65.56%) and left-sided PPV in 198 patients, regardless of gender.

Figure 1 shows vertigo events observed in the period 2000–2004. Clearly evident is the cyclic presentation, with a winter increase in attacks (in January) and a progressive decrease in attacks in spring and summer (minimum in August). In Figure 2, monthly frequency is correlated to nitric monoxide values (in milligrams per cubic microgram), and Figure 3 correlates attack frequency and ultrafine particles of pollution (parts per million [ppm]). In the latter two figures, a direct correlation seem to be evident; even a shift of phase is observed between the events curve and pollution factor curves. Figure 4 displays a monthly trend of events and temperature variations, and Figure 5 regards sun radiation in the

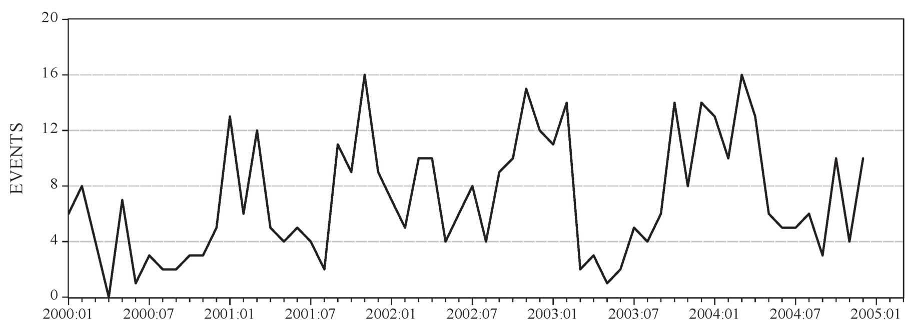

Figure 1. Monthly trend of seasonal events from 2000 to 2004. A winter increase of vertigo attacks, with peaks in January, and progressive decrease in attacks in spring and summer, with a minimum in August, is quite evident.

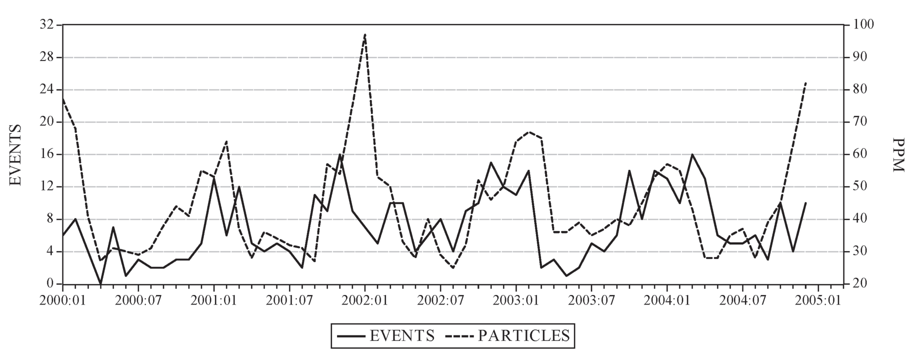

Figure 2. Monthly trend of events from 2000 to 2004 correlated to ultrafine particles pollution (ppm) in the greater Milan area. Trends of the two curves are very similar.

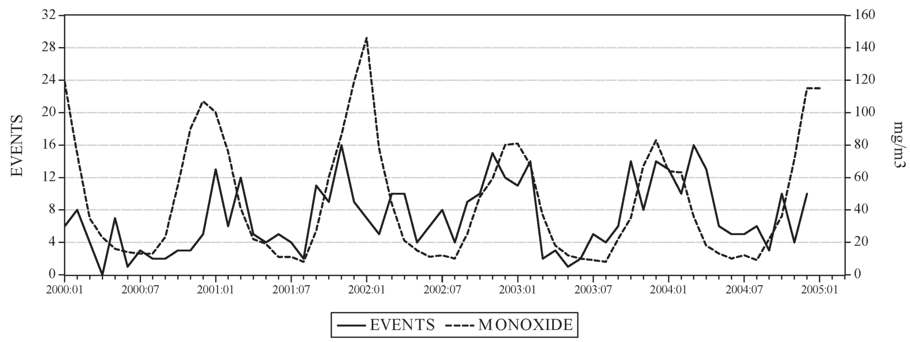

Figure 3. Monthly trend of events from 2000 to 2004 correlated to nitric monoxide values (in mg/mc^3) in the greater Milan area. Trends of the two curves are very similar.

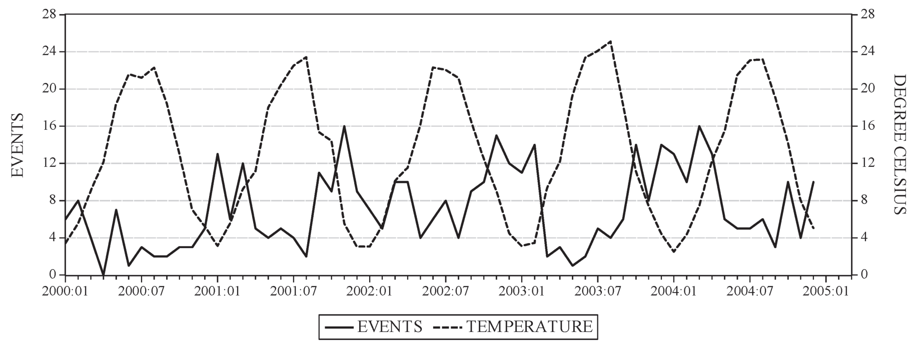

Figure 4. Monthly trend of events from 2000 to 2004 correlated to temperature variations in the greater Milan area. The two curves present an inverted correlation.

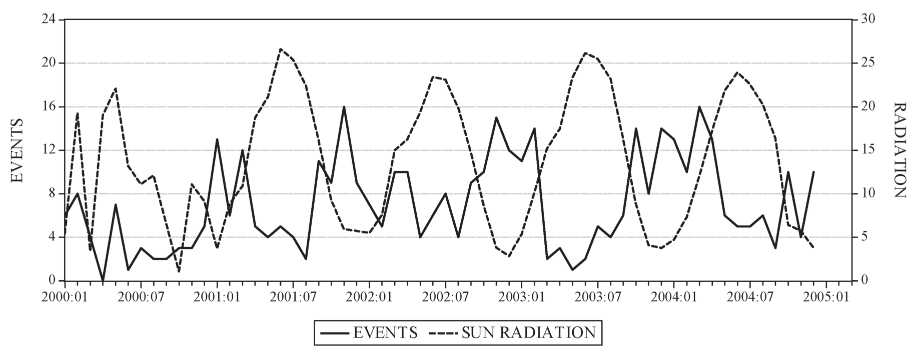

Figure 5. Monthly trend of events from 2000 to 2004 correlated to sun radiation variations in the greater Milan area. The two curves present an inverted correlation.

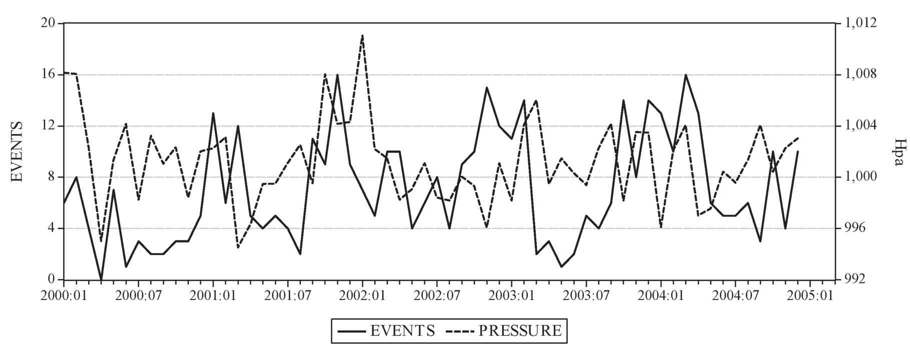

Figure 6. Monthly trend of events from 2000 to 2004 correlated to air pressure in the greater Milan area. The two curves are not correlated.

greater Milan area. In both cases, the two curves seem to present an inverted correlation. Figure 6 shows a monthly trend of events correlated to air pressure, and Figure 7 shows humidity in the greater Milan area. In the latter two figures, the two curves do not seem to be correlated.

We conducted descriptive statistics for the two variables—temperature and particles—that appear to be more correlated than the others to PPV events (Table 1). These two variables are significantly correlated ($p <$ .01). Temperature has the highest correlation in absolute

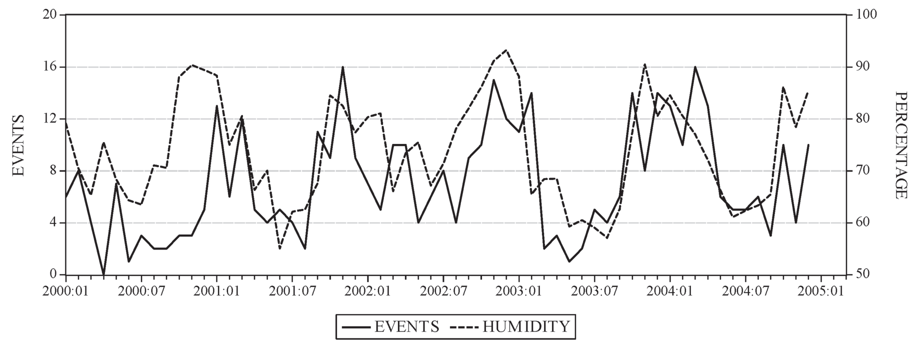

Figure 7. Monthly trend of events from 2000 to 2004 correlated to air humidity in the greater Milan area. The two curves are not correlated.

value with particles (0.732). Events and particles show a correlation of 0.304: An increase in particles signals a major incidence of patients' experiencing PPV ($p < .05$). The correlation between events and temperature is -0.552: When temperature decreases, PPV events increase ($p < .01$).

Table 1 suggests the presence of linear relations between the pairs of variables event-temperature and event-particles. To better understand this evidence, we have conducted a regression analysis, the results of which are summarized in Tables 2–5. All these tables report the regression coefficients and the relative standard errors, *t*-statistics and *p*-values. When the Durbin-Watson statistic was below 1.5 (i.e., possible residual autocorrelation), we computed standard errors (and thus *t*-tests) robust to the presence of autocorrelation in the regression

Table 1. Correlation Matrix with Significances

	Events	Particles	Temperature
Events	1.000	0.304	−0.552
p-Value	—	0.018	0.000
Particles	0.304	1.000	−0.732
p-Value	0.018	—	0.000
Temperature	−0.552	−0.732	1.000
p-Value	0.000	0.000	—

Table 2. Regression of the Monthly Number of Events on Average Temperature

	Coefficient	SE	*t*-Statistic	*p*-Value
Intercept	11.303	1.133	9.977	0.000
Temperature	−0.324	0.056	−5.779	0.000
R-squared	0.305	Schwarz criterion		5.477
Adjusted R-squared	0.293	Durbin-Watson statistic		1.489
SE of regression	3.555	*F*-statistic		25.449
Log likelihood	−160.213	Prob (*F*-statistic)		0.000

Note: Standard errors (SE) are robust to residual autocorrelation.

Table 3. Regression of the Monthly Number of Events on Average Level of Particles

	Coefficient	SE	*t*-Statistic	*p*-Value
Intercept	3.446	1.527	2.257	0.028
Particles	0.082	0.028	2.893	0.005
R-squared	0.093	Schwarz criterion		5.744
Adjusted R-squared	0.077	Durbin-Watson statistic		1.377
SE of regression	4.062	*F*-statistic		5.917
Log likelihood	−168.219	Prob (*F*-statistic)		0.018

Note: Standard errors (SE) are robust to residual autocorrelation.

Table 4. Regression of the Monthly Number of Events on Average Temperature and Particle Level

	Coefficient	SE	*t*-Statistic	*p*-Value
Intercept	15.087	3.425	4.405	0.000
Temperature	−0.417	0.100	−4.177	0.000
Particles	−0.058	0.041	−1.425	0.160
R-squared	0.327	Schwarz criterion		5.514
Adjusted R-squared	0.303	Durbin-Watson statistic		1.487
SE of regression	3.530	*F*-statistic		13.819
Log likelihood	−159.273	Prob (*F*-statistic)		0.000

Note: Standard errors (SE) are robust to residual autocorrelation.

Table 5. Regression of the Number of Monthly Events on a Linear Trend, Average Temperature and Average Particle Level

	Coefficient	SE	*t*-Statistic	*p*-Value
Intercept	13.758	3.047	4.516	0.000
Linear trend	0.081	0.023	3.547	0.000
Temperature	−0.449	0.082	−5.487	0.000
Particles	−0.072	0.038	−1.876	0.066
R-squared	0.436	Schwarz criterion		5.404938
Adjusted R-squared	0.406	Durbin-Watson statistic		1.775910
SE of regression	3.259	*F*-statistic		14.422
Log likelihood	−153.959	Prob (*F*-statistic)		0.000

errors. This precaution has to be taken since time series regressions often suffer from residual autocorrelations and the standard errors estimated through ordinary least square methods may yield inconsistent results. In the lower part of the tables, we report the usual goodness-of-fit statistics and the ANOVA F test with p-value. We carried out residual normality tests (Jarque-Bera) as well, which we do not report in this article: In all cases, the hypothesis of normality of the regression errors was supported by the data.

Table 2 reports the results of the regression of the number of monthly events on a constant and the average temperature for each month. As expected from the correlation test in Table 1, temperature is a significant predictor for the number of events and accounts for some 30% of the variability of the phenomenon. In particular, an additional degree (Celsius) in the average temperature is expected to reduce the number of monthly events by 0.32 units.

The results from regressing the number of monthly events on the average level of particles may be read in Table 3. The relation is still significant (at a 5% level), but the predictive power of the particle variable is rather low: it accounts for only 9% of the variability of the number events.

As temperature and particle level show significant negative correlation (-0.732), we cannot discount the possibility that one of the two preceding regressions is spurious. In fact, the number of events may depend only on temperature but not on particle pollution or vice versa, and the significance of both regression could be ascribed to the strong relation between temperature and pollution. To control for the reciprocal effect of the two variables, we carried out a multiple regression of the number of events on both temperature and particle level, and these results are reported in Table 4. The regression coefficient of the particle variable is no more significantly different from zero (p-value $= 0.16$), and we may conclude that among the variables we are considering, only the temperature is a predictor for the number of events.

In the last regression, summarized in Table 5, we tried to assess whether the number of events tends to grow over time, by including a linear trend among the predictors. Though the conclusion about the effect of particle pollution remains unchanged (the regression coefficient is not significantly different from zero), a slight tendency for the events to appear more frequently as time passes proved significant. More precisely, the events seem to increase by 0.08 units every month, which equates to approximately one additional event every year. This is truly not a negligible figure if we consider that in our sample the average monthly number of events is 7.

Finally, in every regression we ran, we considered the possibility of an August effect (because in Italy, this may be important), but such an effect never proved to be statistically significant.

DISCUSSION

PPV is widely accepted as a labyrinthine disease. The hypothesized cause of PPV is dislodgement of small calcium carbonate crystals that float through the inner-ear fluid and strike against sensitive nerve endings within the balance apparatus at the end of each semicircular canal. These crystals usually dissolve or fall back into the vestibule and no longer cause any symptoms. However, in some patients, these crystals could be trapped in the endolymph and cause symptoms, as gravity and head movements cause them to repeatedly strike against the cupula.

In our group of patients, PPV was prevalent in women and also showed a right-sided prevalence regardless of gender. Both female and right-sided prevalence have been observed previously [1,2,7]. The female preponderance among patients with PPV has been hypothesized to be correlated with migrainous vertigo [8], but the link to migraine is not fully understood.

Female prevalence has been correlated by Vibert et al. [9] to osteopenia and osteoporosis. The diagnosis of osteopenia or osteoporosis was confirmed by a bone mineral density measurement made with dual x-ray absorptiometry of spine and hip (T-score). Results showed osteopenia or osteoporosis in 75% of considered cases. The T-scores were compared to those of 83 healthy women, revealing that the patients with PPV had a significantly lower T-score ($p < .026$). The authors hypothesized an influence of calcium metabolism dysregulation on otolith metabolism, with an increased trend to otoconia debris formation [9].

Right-sided prevalence was discussed by Cakir et al. [10]. Those authors found that the ear affected by PPV was, in 86% of cases, consistent with the side of the head on which the patient was lying during bedrest. Thus, these authors concluded that habitual lateral head positioning during bedrest could be a major factor leading to the development of PPV in the ipsilateral ear.

Regarding seasonality, results clearly show that PPV, even if present throughout the year, is strictly correlated to winter. Several studies have shown that atmospheric conditions can affect well-being or disease and that some individuals seem to be more sensitive to weather than others. As epidemiological data on the prevalence of weather-related health effects are lacking, two representative weather sensitivity surveys were conducted independently in Germany and Canada. The highest frequencies of weather-related symptoms were reported in Germany for stormy weather (30%) and increasingly cold weather (29%). In Canada, mainly cold weather

(46%), dampness (21%), and rain (20%) were considered to affect health more than other weather types [11]. Even if an influence of disorders of circulation or metabolism (or both) on the inner ear or otoconia metabolism might be suspected, it is noteworthy that, on multivariate analysis, hypertension, hyperlipidemia, and stroke were independently associated with PPV [12]. Thus, the mechanism through which season or weather could influence well-being in general and inner-ear metabolism in particular is not yet clearly understood.

Patients with PPV reported significantly more life-changing events than did control subjects in the year preceding the onset of vertigo [2]. Negative life events, objective negative impact, and a poor degree of control were also significantly more frequent in patients as compared with controls. Monzani et al. [2] reported that psychometric questionnaires recorded significantly higher levels of anxiety, depression, and somatization in the pathological sample and an increased obsessive-compulsive attitude. A possible speculation is that seasons could interfere with the psychological attitude of some patients. Regarding climate, air humidity and pressure are not correlated to a PPV trend, whereas temperature and, obviously, sun radiation significantly influence PPV frequency.

Possibly temperature influences endolymph metabolism directly or through pollution. Nitric monoxide is slightly correlated to PPV frequency, whereas particle pollution seems to be more strictly correlated, although statistical analysis is not definitively clear enough (see Table 5) to attribute to particles a role in PPV trends. Nemmar et al. [13] showed passage of inhaled particles into the blood circulation. Nel [14] pointed to accumulating evidence that absorbed particles through alveolar membranes provide a template for electron transfer to molecular oxygen in reduction and oxidation cycling cellular events. Failure to overcome oxidative stress leads to the activation of intracellular cytokine and chemokine, produced locally in target tissues as well as systematically, leading to widespread pro-inflammatory effects remote from the site of damage. Some individuals may be more prone to development of inflammation.

Raponi et al. [15] have described the role of oxidative stress in Ménière's disease. Then, oxidative stress could be a factor able to induce disorders in otoconia metabolism because orchestration of extracellular biomineralization requires bringing together ionic and proteinaceous components in time and space. Normal generation of otoconia requires a complex temporal and spatial control of developmental and biochemical events [16] that could be disrupted by oxidative stress induced by particles and nitric monoxide gaining access to the systemic circulation by penetrating alveolar membranes in lung tissue. During periods of increased air pollution, in some individuals—probably those not able to counteract oxidative stress—the activation of cytokine and chemokine produces endolymphatic free-floating debris.

The effect of inhaled toxic agents could be less clear. In fact, Sunami et al. [3] faced the question of whether the length of time until recovery was influenced by cigarette smoking. Those authors observed that smoking was associated with a lower incidence of benign paroxysmal positioning vertigo and that patients without recurrence were more frequently smokers than patients with recurrence. Finally, the authors reported that, paradoxically, there was a tendency for smoking patients to recover sooner than nonsmoking patients.

CONCLUSIONS

PPV is more frequent in middle-aged women (in and around their fifties) and is more likely to be right-sided. PPV is clearly correlated to the winter season, and the frequency of attacks depends on temperature variations. The role of air pollution, especially particles, is suspected but has not yet been clearly identified. The factors that link climate and otoconia metabolism require further investigation.

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