Seasonal Variation in Cryptogenic and Noncryptogenic Hemoptysis Hospitalizations in France*

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Study objective: To determine the potential role of seasonality in hospitalizations for cryptogenic and noncryptogenic hemoptysis in the French population.

Design: Retrospective analysis of hospital discharge data from a National Register.

Setting: All 29 French university hospitals, between July 1, 1994, and June 30, 1997.

Patients: Two thousand six hundred seventy-seven and 3,672 adult hospitalizations for cryptogenic and other hemoptysis, respectively.

Measurements: Cumulative monthly averages were determined, expressed as the percentage above or below the average monthly value during the entire study period.

Results: The distribution of cumulative monthly hospitalizations for cryptogenic hemoptysis peaked in March (32% above the average) and was lowest in summer (30% below the average; p < 0.001). Hospitalizations for noncryptogenic hemoptysis followed a similar seasonal pattern (p < 0.001). In the 16- to 34-year-old individuals, cryptogenic hemoptysis, compared with noncryptogenic hemoptysis, showed a higher incidence with a larger seasonal amplitude (p < 0.001).

Conclusions: A better understanding of the fundamental pathophysiologic mechanisms underlying this respiratory and hemorrhagic condition may be helpful in developing preventive measures, especially in patients with a risk of recurrence.

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Key words: hemoptysis; hospitalization; seasons

Abbreviation: ICD = International Classification of Diseases

Hemoptysis is considered a sign of serious disease (e.g., tuberculosis, lung cancer, acute bronchitis, pneumonia), and recurrent or abundant episodes produce a potentially life-threatening situation.

The epidemiology of hemoptysis has changed since the control of tuberculosis in developed countries.1–3 Search for lung cancer now predominates in management strategies.4 However, despite modern diagnostic means, the cause goes undetected in nearly a third of all cases of hemoptysis.5

Adelman et al5 investigated cryptogenic hemoptysis and reported that bronchial inflammation and infection were the most frequently suspected causes. The clinical observation that patients with cryptogenic hemoptysis presented most often during the winter months supported this hypothesis, but the difference was not statistically significant in this small series.

For editorial comment see page 288

We studied a large sample of French adults to determine whether hospitalization for cryptogenic hemoptysis follows a seasonal pattern different from noncryptogenic hemoptysis.

Materials and Methods

Study Population

We analyzed retrospectively the French teaching hospital discharge register between July 1, 1994, and June 30, 1997. This data set includes all discharges from all teaching hospitals in
France: These 29 teaching hospitals represent 47,531 short-stay/acute-care beds, or 28.3% of public-hospital capacity in France in 1996.

The Anonymous Hospital Discharge Data Set is abstracted from information collected at discharge from patient medical records. The rules of the database exclude redundant entries when a patient is transferred from one unit to another for the management of the same hemorrhagic event. This information includes age, sex, and month of discharge, with space for up to 99 medical diagnoses and 99 procedures. The database contained 7,892,324 recordings for the study period.

Owing to confidentiality measures, these data could not be linked by patient. Repeat admissions for the same patient during the 3 years were not investigated.

**Case Definition**

Medical diagnoses were classified according to the Internationla Classification of Diseases (ICD)-9 until 1996, and the ICD-10 in 1997 and thereafter.

Inclusion of hospitalizations for hemoptysis was based on a four-digit ICD diagnostic code of 786.3 (ICD-9) and R04.2 (ICD-10). Hospitalizations are reported from all listed discharge diagnoses.

We excluded children and adolescents < 16 years of age \((n = 143)\) and, on the basis of the associated diagnoses, hospitalizations for traumatic hemoptysis \((n = 1,193)\).

Hemoptysis was categorized as noncryptogenic hemoptysis on the basis of the associated diagnoses of lung cancer, bronchiec-tasis, chronic bronchitis, acute bronchitis or pneumonia, and miscellaneous well-known causes. In the absence of the above diagnostic codes, hemoptysis was classified as cryptogenic hemoptysis.

### Table 1—Hospitalizations for Cryptogenic Hemoptysis and Noncryptogenic Hemoptysis From July 1994 Through June 1997, Numbers, and Seasonal Variation for All Cases, by Sex and by Age

<table>
<thead>
<tr>
<th>Variables</th>
<th>Cryptogenic</th>
<th>Noncryptogenic</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hospitalizations, No.</td>
<td>2,677</td>
<td>3,672</td>
</tr>
<tr>
<td>%</td>
<td>100.0</td>
<td></td>
</tr>
<tr>
<td>Seasonal variation*</td>
<td></td>
<td></td>
</tr>
<tr>
<td>January</td>
<td>11</td>
<td>5</td>
</tr>
<tr>
<td>February</td>
<td>12</td>
<td>20</td>
</tr>
<tr>
<td>March</td>
<td>32</td>
<td>42</td>
</tr>
<tr>
<td>April</td>
<td>20</td>
<td>23</td>
</tr>
<tr>
<td>May</td>
<td>-2</td>
<td>5</td>
</tr>
<tr>
<td>June</td>
<td>5</td>
<td>-12</td>
</tr>
<tr>
<td>July</td>
<td>-23</td>
<td>-31</td>
</tr>
<tr>
<td>August</td>
<td>-30</td>
<td>-43</td>
</tr>
<tr>
<td>September</td>
<td>-23</td>
<td>-41</td>
</tr>
<tr>
<td>October</td>
<td>-6</td>
<td>1</td>
</tr>
<tr>
<td>November</td>
<td>0</td>
<td>25</td>
</tr>
<tr>
<td>December</td>
<td>3</td>
<td>-2</td>
</tr>
<tr>
<td>Total seasonal variation†</td>
<td>62</td>
<td>85</td>
</tr>
<tr>
<td>Roger’s test</td>
<td>&lt; 0.001</td>
<td>&lt; 0.001</td>
</tr>
</tbody>
</table>

*Percent above or below the average monthly value for the entire study period.
†Sum of the percentage above the average for the month with the highest value and the percentage below the average for the month with the lowest value.
tions (15.5%), hemorrhagic diathesis (11.8%), and systemic diseases (1.7%). These causes totaled 3,672 cases of noncryptogenic hemoptysis (57.8% of all hemoptysis cases). Finally, in the absence of the above diagnostic codes, 2,677 cases of hemoptysis were classified as cryptogenic (42.2% of all hemoptysis cases), giving a monthly average of 74,618 hospitalizations.

The distribution of cumulative monthly hospitalizations for cryptogenic hemoptysis showed a significant seasonal variation with Roger’s test (p < 0.001). Average monthly admissions (Table 1 and Fig 1) differed by as much as 62%, ranging from a peak 32% above average in March to 30% below average in August.

This seasonal pattern of hospitalizations for cryptogenic hemoptysis was influenced by age and not by sex. The amplitude of the seasonal variation in hospitalizations was greater among patients 16 to 34 years of age than among patients ≥65 years. Total seasonal variations fell with age, from 85 to 58% and 53% in the three selected age groups (16 to 34 years, 35 to 64 years, and ≥65 years).

Hospitalizations for noncryptogenic hemoptysis (n = 3,672, 102 ± 30/mo) followed a similar seasonal pattern, with a seasonal variation of 49% (Table 1 and Fig 1). Cryptogenic hemoptysis and noncryptogenic hemoptysis exhibited the same distribution across months and sex. Only the distribution by age differed between the two conditions (19.2% of persons in the 16- to 34-year age range with cryptogenic hemoptysis vs 8.9% for noncryptogenic hemoptysis; p < 0.001).

Discussion

Several main findings emerged from this study. First, spontaneous cryptogenic hemoptysis necessitating hospitalization in France peaked in late winter and early spring (peak in March), both in the overall population and in subgroups defined by age and sex. Second, patients with cryptogenic hemoptysis were younger than those with noncryptogenic hemoptysis, and for persons 16 through 34 years of age, cryptogenic hemoptysis hospitalizations exhibited a larger seasonal amplitude. Third, hospitalizations for noncryptogenic hemoptysis followed a similar seasonal pattern, suggesting probably common triggering factors.

The only previous mention of seasonality regarding hemoptysis is in the report by Adelman et al,5 in which the winter predominance (not statistically significant) of cryptogenic hemoptysis was cited to support the infectious hypothesis. The seasonal variation of noncryptogenic hemoptysis is similar to that of a number of other pulmonary disorders,6,8 a number of which (exacerbations of bronchiectasis and chronic bronchitis, acute bronchitis or pneumonia) are quite well established as major causes of hemoptysis, and could be triggered by winter-predominant respiratory pathogens.9,10

Apart from infection, cold is another potential triggering factor of cryptogenic hemoptysis. Several investigators have documented an increase in respiratory and cardiovascular morbidity and mortality during cold weather.11–14 Cold weather has been found to correlate with hemorrhagic events in pa-

Figure 1. Monthly percent variations in hospitalizations for cryptogenic hemoptysis and for noncryptogenic hemoptysis. The reference value, which is the average monthly value, is 0%. Data points represent cumulative data from July 1994 through June 1997.
tients with hemophilia, and with an increase in the incidence of primary intracerebral hemorrhage and subarachnoid hemorrhage. It should also be noted that hospitalizations for epistaxis are more frequent during dry and cold winter months.

The link between cold and morbidity may not be causal, low temperatures simply being a surrogate measure for related factors (transmittable agents or environmental factors). Reasonable proof of an environmental influence comes from the reversal of seasonality of mortality (total, cardiovascular, and respiratory) in the Southern Hemisphere. Seasonal variations in other factors, such as atmospheric pollution, other meteorologic factors, exposure to sunlight, use of nonsteroidal anti-inflammatory drugs, and dietary intake (notably vitamin C), may also be involved.

Our percentage of lung cancer (14.9%) could seem low compared with the US experience. In Israel, Hirshberg et al also found a low percentage of cancer cases (19%). According to these authors, the finding of bronchiectasis as a main cause for hemoptysis (20%) is probably secondary to remote nonactive tuberculosis infection (acquired during or just after World War II) or other infections.

It could be argued that using teaching hospital discharge data might induce some selection bias. In France, as hemoptysis is relatively uncommon and generally perceived, by both patients and physicians, as a serious condition, it leads to immediate hospital admission and etiologic investigations (thoracic CT scan included), lending weight to the value of hospital files. This is particularly true in countries like France that have universal health care, as virtually the entire population is covered. Misclassification biases are probably minor in studies of such a disease condition that is easy to diagnose and code.

Establishing the diagnosis of cryptogenic hemoptysis in the absence of a diagnostic code indicating a likely cause for hemoptysis might also introduce some bias. Because of the multicenter, nationwide nature of this large database and confidentiality measures, we were unable to review all or only a sample of medical records to validate the appropriateness of the coding. The cryptogenic diagnosis is, however, one of elimination; in a teaching hospital, it is made by specialists and usually backed up with bronchofibroscopy and thoracic CT scan. In addition, mandatory quality control checks are performed every 6 months by the medical information department of each hospital and every year by physicians from the governmental authorities and the national health insurance system.

Another potential limitation is that our databases do not collect information on all pulmonary and cardiovascular risk factors or possible precipitating factors for relationship between season and hemoptysis.

Possible selection biases related to seasonal population variations were limited by the multicenter, nationwide nature of this large database. Because the number of foreigners visiting France in summer is about four times that of French people going abroad, the lower rate of summer hospitalization for hemoptysis would not be linked to a vacation-related reduction in the at-risk population.

**CONCLUSION**

The seasonal periodicity of cryptogenic and non-cryptogenic hemoptysis hospitalizations clearly demonstrated by these epidemiologic data showing a peak incidence in winter and early spring months, has important implications. Future questions include whether it might be advisable to inform susceptible patients of the increased risk during winter and early spring. Further community-based or prospective studies are required to better understand the fundamental pathophysiologic mechanisms underlying this respiratory and hemorrhagic condition. Identification of significant environmental factors (infection, cold, etc.) or other triggers (drug-induced coagulation abnormalities) could be useful for practitioners to improve causative prevention measures and educational strategies, especially in patients with a risk of recurrence.

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