

Epidemiology of asthma in western Europe

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Asthma deaths are uncommon, but have recently increased in some countries due to problems in the management of the disease. Morbidity rates show large variations, which can be attributed to differences in defining the disease, but also to genuine variations, with a trend towards less asthma in northern Europe. It has been suggested that allergic diseases as a whole, and asthma in particular, may exhibit an upward secular trend. Risk factors include a genetic background and environmental triggering factors. The importance of genetic factors is illustrated by family studies and by extreme prevalence rates observed in some communities. Environmental factors include rapid air pollution variations which act as a trigger for asthma attacks. However, at levels currently prevailing in western Europe, air pollutants do not induce a higher incidence of asthma. Altitude generates a gradual decrease in *Dermatophagoides*, thus explaining both the clinical improvement in asthmatics living in altitude and a lower prevalence of asthma in populations born and living there. Among the other aero-allergens, grass pollens plays a major role in spring, eliciting asthma attacks. Some natural allergens transformed by man (castor bean, soja) can be responsible for asthma epidemics.

Key words: asthma; environment; epidemiology; genetic.

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Epidemiological study of asthma includes:

- Descriptive epidemiology, i.e. mortality and morbidity in relation to asthma, and disease distribution according to personal characteristics.
- Analytical epidemiology in search of risk factors. We will consider, among intrinsic factors, atopy and hyperreactivity, and among extrinsic risk factors, air pollution and meteorological conditions, and allergen exposure.
- Experimental epidemiology, i.e. preventive and therapeutic interventions, which will not be considered in this review. However, they can be inferred from knowledge of extrinsic risk factors.

ASTHMA AS A PUBLIC HEALTH PROBLEM

Mortality rate is not a sensitive index because deaths from asthma are uncommon. The death

rate in countries where mortality figures are reliable is low, ranging from 0.4 to 4.0 deaths per 100,000 subjects per year, for the age range 5 to 34 years old (86). For example, in France in 1986 there were 2,402 deaths attributed to asthma. However, from 1961 to 1967, especially in Great Britain, this rate increased three-fold. This increase in death rate generated in 6 years 3,000 extra deaths. Beta-adrenergic sprays, marketed in Europe since 1960, have been charged with this extra mortality (75). In New Zealand, the same increase was noticed at the same time and is still going on (43). In the United States recent reports have indicated a rapid increase in asthma deaths, especially among black teenagers (57, 69). The same increase has been recently noted in the United Kingdom (7). The reality of this increase has been questioned. It appears partly related to the change in the International Classification of Diseases, which occurred in 1969, and to the better awareness of the disease, but the increase

is a true one. The hypotheses for this increase included disregard of perceived asthma symptoms, non-compliance with the medical regimen, denial of overall seriousness of the disease, significant psychosocial problems in the family, delay in seeking help, confusion about therapy, and over-reliance on bronchodilator therapy without seeking additional therapy with corticosteroids.

Morbidity rate is evaluated in terms of prevalence rate (proportion of patients in a given population, at a given time) rather than in terms of incidence rate (number of new cases arising in a given population in a given period) because it is often difficult to identify the beginning of the disease. There are large variations in morbidity rates in published studies. These variations are partly due to differences in defining the disease, and partly to the characteristics of the population under study.

Prevalence rates depend on criteria for diagnosis

In epidemiology, the diagnosis of asthma relies mainly on answers to standardized questionnaires; sometimes the questionnaire is supplemented by pulmonary function tests. The questionnaire includes either a diagnostic question: "Have you ever had asthma?", or questions about asthmatic symptoms. The diagnostic question is more direct but answers are influenced by the medical knowledge conveyed from the physician to the patient and by the picture of the disease in the population. Questions about symptoms may be less biased, but their sensitivity and specificity must be checked. The questionnaire set up by the British Medical Research Council (BMRC) in 1976 includes the following questions: "does your chest ever sound wheezing or whistling?", "have you ever had attacks of shortness of breath with wheezing?" and, in the "Past illnesses" section an inquiry about "bronchial asthma". In the 1978 American Thoracic Society questionnaire (30), the wording is slightly different. The first question is: "does your chest ever sound wheezy or whistling?", the second: "have you ever had an attack of wheezing that has made you feel short of breath?" and the third, in the "Past ill-

nesses" section: "have you ever had asthma?". The European Coal and Steel Community questionnaire includes three consecutive questions devoted to the diagnosis of asthma: "have you ever had wheezing in your chest?", "have you ever had attacks of shortness of breath with wheezing in the chest?", and "have you ever had asthma attacks?". Because of subjectivity inherent to questionnaires, other tests have sometimes been included in epidemiological studies: measure of serum immunoglobulin E (IgE) level, determination of serum or nasal eosinophilia and, above all, pulmonary function tests. Between attacks, pulmonary function, evaluated by spirometry, is often normal in asthmatic subjects. Thus bronchial provocation tests are useful. However they are time-consuming; even the rapid method developed by Woolcock et al. takes 25-30 min to complete (87).

In children, through the various studies performed around the world and reviewed by Gregg (31), 7 to 25% of persons have had wheezing in their chest, but only 0.7 to 5% have had asthma, according to answers to questionnaires. Some epidemiological studies (53, 85) suggest that wheezy bronchitis is close to asthma because both have underlying bronchial hyperreactivity and respond well to bronchodilators. This pooling does not apply to infants in whom any aggression can induce wheezing attacks without predictive value for subsequent asthma.

Similarly, in adults, acute infection in chronic bronchitis often give rise to wheezing. Thus, diagnosis between asthma and wheezy bronchitis is often difficult. In London, 28% of the men and 22% of the women have had wheezing in their chest; in the Netherlands, 31 and 20% respectively. For asthma the prevalence rate ranges from 1.1 to 9.9% in published studies (31). The broadness of this estimate lies partly in the questions used to identify asthma. In a recent epidemiological study performed in south-east France, Dor (23) studied 29,000 army recruits. According to a self-administered questionnaire, 7.2% answered yes to the question: "have you ever had asthma?", while only half of them, i.e. 3.6% answered yes to questions about asthma attacks, attacks of breath-

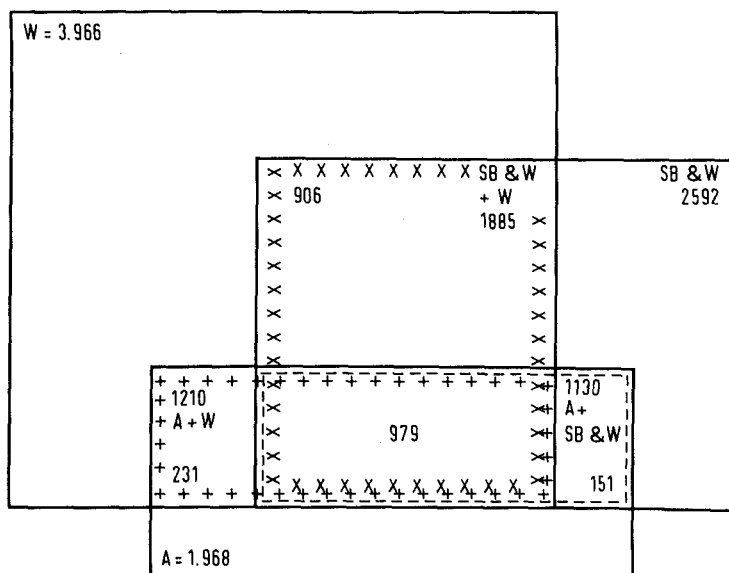


Fig. 1. Distribution of answers to questions about asthma in a survey performed in 29,000 army recruits (23). 979 subjects, i.e. 3.6% of the group, answered yes to all three questions. W: wheezing; SB & W: shortness of breath with wheezing; A: asthma.

lessness with wheezing in the chest, and about wheezing in the chest (Fig. 1). One per cent answered yes to the question about asthma and attacks of breathlessness with wheezing but denied having had wheezing in the chest!

Finally, prevalence figures depend on considering period prevalence (past or present asthma) or point prevalence (present asthma only). In the former case, the figure is higher and the knowledge about the disease in a population is better, but the rate is underestimated because remote attacks may have been forgotten.

Prevalence rates depend on individual characteristics

In children the *male/female ratio* varies, in published studies, from 1.3/1 to 3/1. As occupational and smoking factors do not interfere at this age, males seem to be more susceptible to asthma. This susceptibility could be related to a lower value of the ratio of airways caliber to lung volume in boys (33). By contrast, in adults, the disease is equally distributed in both

sexes. The clinical feeling of a predominance of late asthma in women arises probably from the fact that wheezing in smoking middle-aged males calls to mind the diagnosis of chronic bronchitis.

Prevalence rates are very dependent on *age*. Wheezy bronchitis is quite common in infants, but, as we said above, its predictive value for future asthma is poor, unless there are: a history of familial atopy, atopic eczema or a high serum IgE level. Usually asthma starts around 5, in both boys and girls. Youth is a strong predisposing factor, especially in children born into allergic families. In 1,106 clinic patients with marked skin reactions (61) onset of asthmatic symptoms occurred under 10 in over half of the cases, under 20 in over three-quarters of the cases. One time out of three, asthma subsides at puberty, somewhat sooner and more often in girls than in boys. These data are derived from Rackemann's study (70). This author followed up, prospectively, 459 persons during 20 years: of 459 children who had had asthma before 13 years old, 30% had a quies-

cent asthma 20 years later. In a prospective study of asthma in the rural community of Lebanon (Connecticut), Schachter et al. (73) accounted 73 active asthmatics in 1972 (out of a population of 1,303 white residents). Six years later, in 1978, 50 (68%) were in remission. This improvement occurred in adults as well as in children. A second peak in asthma prevalence occurs around 50, these late asthmas are usually more severe. However, even in those cases long-term prognosis is unforeseeable. In women especially, once menopause is over, asthma attacks may diminish and even disappear.

According to the published studies asthma is unevenly distributed *globally*. These discrepancies may be partly due to differences in methodology. In children (Table 1), prevalence rates are low in Scandinavian countries (between 0.5 and 2.0%), medium in France, Great Britain and Portugal (between 1.8 and 4.8%). In university students, the prevalence rates (9) are usually higher than in the general population, which could be due to a higher socio-economic status in these groups. Similarly, in adults, prevalence rates are very scattered (Table 2). The upper extreme figures are found in Tristan da Cunha island (South Atlantic). The proportion of active asthma was 22% in 1971 while the cumulative

prevalence was 32% (17). The lower figures were recorded in Esquimos. Hospital files from Mackensie delta (Northwest Territories, Canada) include, over a 12-year period, three asthma cases only! Such differences in prevalence figures suggest the intervention of genetic factors which we will analyse later.

Social class may act on asthmatic risk through living conditions, occupational exposure or through health education or health care accessibility. Relationships between social class and prevalence rate of asthma remain unclear. The Tecumseh (Michigan) study (5) concluded that asthma was more prevalent in high social classes; but Higgins (39), in a sample of 4,699 men and women taken from this same community did not find any correlation between asthma prevalence and occupation or education.

Morrison-Smith & Springett (64) evaluated the relationship between a child's *month of birth* and his subsequent risk for bronchial asthma. This risk seems to be higher when the birth occurs between May and October, and could be related to allergy to house dust and *Dermatophagoides pteronyssinus* (16). Other authors have confirmed these data and concluded that atopic parents should be given a "Christmas pill"!

Table 1
Intercountry variations in infantile asthma prevalence

Country	Age class (years)	Authors	Year of publishing	Prevalence rate (%)	Reference
<i>Scandinavia</i>					
Sweden		Kraepelian	1954	0.7	48
Norway	7-14	Moeller	1955	2.0	31
Finland		Eriksson-Lihr	1955	0.7	26
	10-19	Alanko	1970	0.5	1
<i>Great-Britain</i>					
Birmingham	5-15	Morrison-Smith	1961	1.8	64
Aberdeen	10-15	Dawson et al.	1969	4.8	22
London	5	Leeder et al.	1975	3.2	54
<i>Switzerland</i>	10-15	Varonier et al.	1970	1.9	79
<i>France</i>					
Bas-Rhin	14-18	Burghard et al.	1979	4.1	6
<i>Portugal</i>					
Algarve region	7-18	Nunes et al.	1987	3.4	66

Study of *secular trends* suggests that, in western countries, asthma could be a more common disease than it used to be. John Morrison-Smith (62) performed, over a period of 20 years, three large prevalence studies in Birmingham, England. Using a similar definition of asthma and similar methods for gathering information, he showed a statistically significant progressive increase in prevalence from 1956-57 to 1974-75. A same increase in asthma prevalence was suggested by Varonier in Geneva (79). However it is difficult to be sure that this increase is real. It may only be related to a better awareness of the disease. In France it has been shown by a large total population survey (52) that between 1970 and 1980 asthma complaints have increased by 32 %. But, at the same time, complaints from all diseases included have increased by 50 %!

RISK FACTORS OF BRONCHIAL ASTHMA

Knowledge of these risk factors is important:
- intrinsic risk factors enable to predict the individual risk of becoming asthmatic.

- extrinsic risk factors can, in some instances, be controlled.

Intrinsic or endogenous factors

The role of *atopy* includes familial or personal history of allergic disorders, skin reactions to inhaled allergens and high serum total-IgE-level.

A first problem when dealing with "allergic disorders" is to know what these words mean. Atopic eczema, allergic rhinitis and hay fever alone should be included. Some authors rank here drug allergy, headache and even food intolerance. Unfortunately, this assimilation creates disorder. Several retrospective studies have shown that asthmatic subjects have, more often than a control group, a *personal history of allergic diseases*. However, how often this association is encountered depends on the type of asthma and on the institution which performed the study. Hendrick et al. (37), in the Allergy and Clinical Immunology Department of the Brompton Hospital in London, found that 2/3 of asthmatics had a personal history of allergic disorders. This percentage was higher among

Table 2
Intercountry variations in asthma prevalence in adults

Country	Age class (years)	Authors	Year of publishing	Cumulative prevalence rate (%)	References
<i>Scandinavia</i>					
Sweden	16-64	Julin et al.	1967	2.0	45
	30-64	Irnell et al.	1968	2.3	42
	35-54	Kiviloog et al.	1974	2.6	46
Finland	40-64	Huhti	1965	1.1	41
	20-59	Alanko	1970	1.8	1
Denmark	> 16	Weeke et al.	1980	5.2	
Norway	16-69	Gulsvik	1979	1.4*	
<i>Great-Britain</i>					
South Wales	20-44	Burr et al.	1975	3.4	8
London	> 12	Fry	1961	2.0	31
<i>France</i>					
Marseille	18-65	Charpin et al.	1988	3.9	11
<i>Italy</i>					
Pisa	16-65	Viegi et al.	1987	5.0	82

*point prevalence

extrinsic asthmatics (70%) than intrinsic asthmatics (48%). By contrast, when the study considered a non-selected general population, as in the Tecumseh study, less than half of asthmatics had such a personal history (5). Few prospective studies have considered the role of allergic diseases for future asthma. In pollinosis, many authors working in a clinical setting have stated that asthma occurs in a range of 22 to 75% (mean 43%) of persons with hay fever. However, allergists tend to see the more serious hay fever cases and may get a distorted picture of the natural history. The Tecumseh Community Health Study (5) showed not only that this bias actually occurred, but also indicated that the cumulative prevalence of asthma following hay fever was considerably lower (29%) than estimated from clinical experience. Hagy & Settippane (34) followed up a group of 903 freshmen of Brown University, New York. They showed that subjects with history of allergic rhinitis had, over a 7-year period, a 6% risk of developing bronchial asthma, while this risk was only 1.3% in people without such a history.

The importance of *familial history of allergic diseases* is demonstrated in several types of epidemiological studies. Familial studies have shown that the prevalence of asthma in asthmatics' parents is higher than in controls (14). This association is encountered mainly in allergic (extrinsic) asthma (74). Inversely, the risk for children of being asthmatic is greater when one of their parents, or certainly both, are themselves asthmatics (14). In Fergusson et al. (29), the risk of early childhood asthma was increased by nearly 2.5 times for boys, whereas parental asthma was unrelated to early asthma in girls. In this latter study, parental eczema, in both sexes, was associated with child eczema, not with asthma. History of asthma in maternal issues seems to exert a greater influence than in paternal (61). Also, the concordance rate of asthma in monozygotic twins is higher than in dizygotic twins (25). Lastly, extreme prevalence rates mentioned above favour the role of genetics in asthma: Tristan da Cunha islanders were all descended from 15 ancestors, three of whom were asthmatics (38).

The predictive value of positive skin tests to common allergens has been evaluated in Hagy & Settippane's study (34). The risk of developing asthma or allergic rhinitis is correlated with the positivity of skin tests to common allergens. For example, the 7-year risk of asthma in this study was equal to 5% if the tests were positive and to 1.5% if they were negative. However, in a cross-sectional study comparing bronchial reactivity in young asymptomatic subjects with or without positive skin tests to aero-allergens, we failed to find any difference between the two groups (13). Thus, it is likely that bronchial reactivity may not be revealed until the skin test-positive subjects have received repeated bronchial stimulations through inhalant allergens.

Several authors have shown the predictive value of a high serum-IgE level. The IgE level is higher in the umbilical cord in infants from allergic issues, as compared to control infants (35, 47). Michel et al. (60) performed a prospective follow-up study and computed the incidence of allergic disease (eczema, wheezy bronchitis) in relation to umbilical cord IgE level. They showed that this level has a higher predictive value for future allergic diseases than a family history of allergic diseases.

Bronchial hyperreactivity is the hallmark of asthma. However, a certain proportion of hyper-responsive subjects are asymptomatic and a number of symptomatic subjects fail to demonstrate hyperresponsiveness (19). Studies in both humans (84) and animals suggest that airway reactivity is a unimodal function, asthmatic subjects representing the most sensitive extreme of the population. Recent studies suggest that bronchial reactivity itself is inheritable. Bronchial reactivity to inhaled metacholine is higher in families of asthmatic patients than in families of normal individuals (55, 77). In children from asthmatic parents, a causal interaction may occur between atopy and bronchial hyperresponsiveness (18).

Extrinsic or environmental factors

These include domestic, occupational and general air pollution; meteorological factors, smok-

ing and allergens; and factors occurring in early childhood and even during pregnancy.

As for *air pollution*, we will only consider general air pollution. Air pollution can in some circumstances induce bronchial asthma, but acts much more often as a triggering factor for asthma attacks.

Short-term repercussions of high peaks of air pollution on bronchial asthma have been demonstrated in several instances in the past years: Meuse Valley (1930), Donora, Pennsylvania (1948), London (1952). During these episodes, asthmatics were not well: for example in Donora, 43% of the general population but 88% of asthmatics felt chest discomfort. In the Gardanne coal basin area, near Marseille, we could demonstrate a correlation between daily sulfur dioxide levels and daily prevalence of wheezing in the chest (10). By contrast, in many studies which considered periods of several months or 1 or 2 years, correlations between air pollutant levels and number of home visits or visits to the emergency room for asthma, provided contradictory results. These discrepancies may be linked to 1) and uneven level of air pollutants in the various studies 2) the intervention of several pollutants in the induction of asthma attacks; in a specified area, the levels of these various pollutants may not vary in the same direction, and 3) the part played by other bronchial aggressors such as allergens or smoking which could disguise the effect of air pollutants.

Is long-term exposure to air pollutants able to induce a bronchial asthma? A single study, performed on American soldiers stationed in Tokyo and Yokohama after World War II (40), clearly demonstrated that asthma could be cre-

ated out of nothing by exposure to a heavy air pollution and disappear when the person was removed from this polluted area. Similar data have been reported by Maternowsky & Mathews (58) about immigrants: new cases of asthma may develop when people live in a more polluted area. However, in this latter situation, air pollution may be associated with allergen pollution as well as with psychological factors to create asthma.

Apart from those caricatural situations where exposure to air pollutants is drastically altered, do people living in high pollutions areas have more asthma? In children, prevalence studies have shown a correlation between levels of air pollutants and prevalence of upper airway infections and of chest wheezing. As for bronchial asthma, data are scanty. Peat et al. (67) in Sydney failed to find more asthmatic children in polluted areas. In adults, similarly, several studies did not find significant differences in prevalence rates of asthma between urban and rural areas (21), or in cities, between polluted and less polluted neighbourhoods (3). However, a large-scale French multicenter prevalence study (76) performed in 1974-1975, did show a higher prevalence of asthma in the most polluted areas, but in men only. In this study, the responsible pollutant was thought to be sulphur dioxide. The above-mentioned negative results may be due to relatively small sample sizes, to lower levels of air pollutants in recent studies, or to differential migration. Asthmatic subjects may choose to live in less polluted areas. Such a migration bias has been demonstrated in Tucson (Arizona) by Lebowitz & Burrows (51): 3/4 of asthmatics found in their study already had asthma before moving to Arizona.

Table 3

Prevalence rates of asthma and related symptoms at sea level (Marseille) and altitude (Briançon) (12)

	Briançon (n = 1055)		Marseille (n = 4008)
Attacks of wheezing	2.8 ± 0.5	NS	3.9 ± 0.4
Attacks of shortness of breath with wheezing	1.8 ± 0.4	P < 0.02	3.1 ± 0.3
Asthma attacks	2.4 ± 0.5	P = 0.025	3.8 ± 0.7
Positive answers to the above 3 questions	1.3 ± 0.3	P = 0.015	2.6 ± 0.2
Asthma diagnosed by a doctor	2.1 ± 0.4	P = 0.33	3.4 ± 0.3

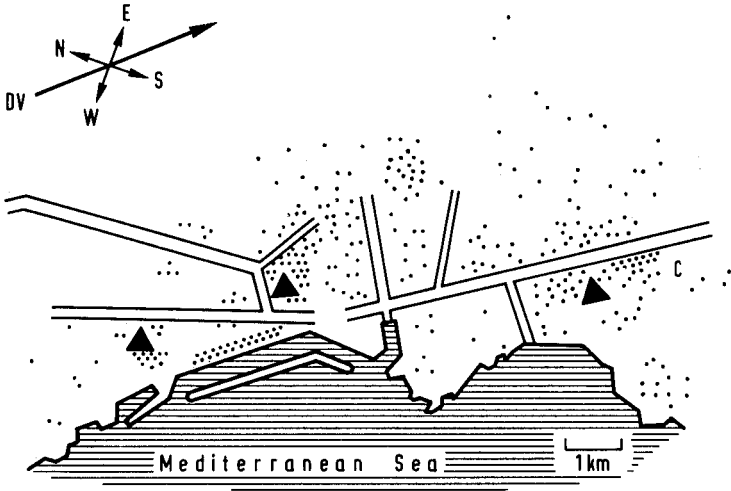


Fig. 2. Epidemic of asthma due to castor bean allergy (15). Dots locate asthmatic patients. Note that they are situated down wind of the oilmill (black triangle). Many cases were concentrated in the block of flats named "C". The ventilation system took in air on the north-east facade, which was down wind of an oil mill. DV: direction of the prevailing wind (mistral).

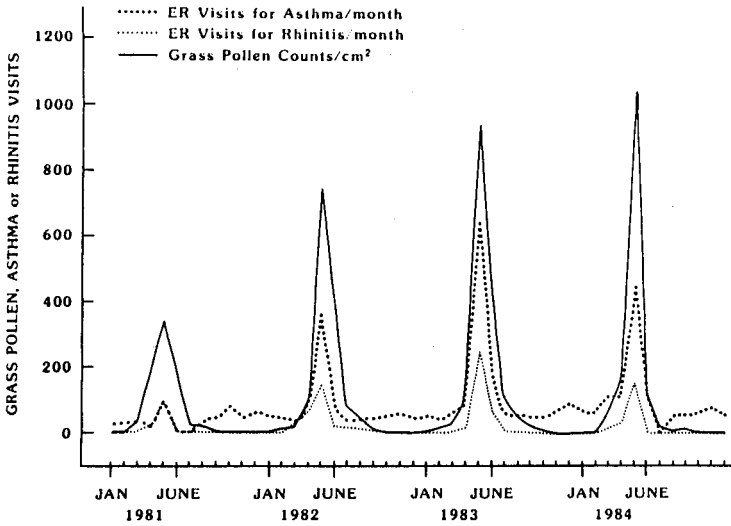


Fig. 3. Correlation between total monthly emergency room visits for asthma and rhinitis and grass pollen counts (71).

Meteorological conditions, apart from cold which acts through a specific mechanism, operate through stagnancy of air pollutants over their sources. Empirically, most asthmatics feel the influence of meteorological factors. Low wind, low barometric pressure, thermal inversions

prevent pollutant dispersion, all the more in sunken valleys. Rapid cooling of whether seems to act as an independent triggering factor. Tromp (78) in the Netherlands, through diaries, showed that atmospheric cooling plays an important role.

This cooling has also been studied by Salvaggio (72) in New Orleans and Cohen (20) in West Virginia. MacFadden and Ingram demonstrated that, in those circumstances, air dryness is more important than air temperature (59).

Another variable included in climatic factors is altitude. Altitude generates a gradual decrease in one of the major allergens: *Dermatophagoides pteronyssinus* (81). This can explain the clinical improvement and the drop in specific IgE to *Dermatophagoides* observed during a prolonged stay at high altitude (80).

Tobacco smoke is a potent bronchial irritant. It can induce asthma attacks, but is it able to create bronchial asthma? As far as active tobacco smoking is concerned, the answer seems to be negative: before the onset of the disease, medical history does not more often include smoking in asthmatics than in a control population. In children, a study by Leeder et al. (54) suggests that passive smoking is responsible for more upper respiratory tract infections and wheezing bronchitis, but does not induce an increase of asthma.

One of the most important seasonal *inhaled allergens* is grass pollen. Some asthmatics may exhibit an exacerbation of asthma in springtime, while, in others, asthma attacks only occur during that period. For example, during spring, curves describing pollen counts and emergency room visits for asthma are parallel (Fig. 3). To be sensitive to such pollens, subjects have to have been previously sensitized. Maternowski & Matthews (58) showed that foreign students living in the United States have a lower prevalence of ragweed allergy when they settle in this country. However, a few years later, this prevalence rate rises to equal the rate prevailing in U.S. students.

Among the perennial allergens, the most important is house dust mite (HDM). Its relevance is supported by strong epidemiological evidence: rapid and parallel increase in asthma prevalence and allergy to HDM in Papua New Guinea populations (24); clinical improvement and fall in specific anti-HDM IgE in asthmatic children who stay in altitude for a few weeks (80); higher prevalence of positive skin test to HDM in children living in humid areas of

British Columbia, compared to dry areas (65). Recently, in a cross-sectional epidemiological study, we compared the prevalence rate of asthma and positive skin tests to *Dermatophagoides pteronyssinus* in a random sample of 4,008 adults 18 to 65 years old living in Marseille on the coast and 1055 people living in Briançon, the highest city in Europe (12). The prevalence rate of asthma and related symptoms was approximately twice in Marseille than in Briançon (Table 3). Similarly, the prevalence of positive skin test to *D. pteronyssinus* was significantly ($P < 0.01$) lower in Briançon (10.2%) than in Marseille (27.0%). We should point out that the studied subjects from Briançon were born, grown-up and living in this town.

Apart from these natural allergens, some other allergens modified by storage or industrial process can be involved in asthma outbreaks. For example, in Marseille in 1955-56 several hundred new cases of asthma in relation to castor bean allergy were noted (15). This allergy had developed because the process of extracting oil from grain had changed and become more drastic, leaving as residuum a powdery oil-cake (Fig. 2). Similarly, Bregevin (4) described asthma related to inhalation of cereal dust in urban dwellings situated near grain-storage units. Recently, in Barcelona, Plasencia et al. described asthma outbreaks related to soya exposure or to a contaminant of the soya grain (68).

The category of *risk factors which occur in early childhood and pregnancy* have recently been extensively studied. Knowledge of these factors could indeed be a basis for asthma and allergy prevention. However, intervention studies during pregnancy, in which pregnant women have been given a diet free of egg and milk, have provided negative results: cord IgE level is not lower in the intervention group than in the control group (27); similarly, the incidence of allergic diseases is not lowered (28). Studies about the potential preventive effect of breast feeding have provided contradictory results (2). These studies are difficult to interpret because the target population can be different (all babies or babies from atopic families), the duration of

breast feeding can vary, breast feeding can be exclusive or not, environmental allergic control may or may not have been implemented. In studies claiming a beneficial effect it has been unclear whether this has been due to avoidance of cow's milk or the positive effect of breast feeding. Johnstone & Dutton (44) claimed an effect using soy formula in the absence of breast feeding while the remaining studies felt breast feeding was primarily important.

Conclusions

Suitable genetic background and environmental aggressors interact to produce clinical bronchial asthma. Genetic background is expressed by bronchial hyperreactivity, which is the permanent and essential hallmark of asthma. However, studies on migrants suggest that if genetic factors are necessary to produce asthma, environmental aggressors, especially if they occur during childhood, have a significant role in the clinical manifestation of asthma. Potent aggressors, such as occupational exposure, can even induce asthma where no previous symptoms had existed.

Knowledge about asthma has been broadened by epidemiology. But, in spite of numerous studies, many grey areas still exist. This comes from the lack of a precise definition of the disease. Bronchial hyperreactivity, as an objective tool, could fill this gap.

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