

# Prevalence of asthma and allergic disorders among children in united Germany: a descriptive comparison

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## Abstract

**Objectives**—To compare the prevalence of asthma and allergic disorders among children in Munich, western Germany, and Leipzig, eastern Germany, where environmental exposure, particularly air concentrations of sulphur dioxide and particulate matter, and living conditions have differed over the past 45 years.

**Design**—Prevalence surveys among school-children aged 9-11 years in Leipzig and Munich. Self completion of written questionnaire by the children's parents and lung function measurements.

**Subjects**—1051 children in Leipzig and 5030 in Munich.

**Setting**—Primary schools.

**Main outcome measures**—Reported lifetime prevalence of asthma and allergic disorders, and bronchial hyperresponsiveness assessed by cold air inhalation challenge.

**Results**—The lifetime prevalence of asthma diagnosed by a doctor was 7.3% (72) in Leipzig and 9.3% (435) in Munich; prevalences of wheezing were 20% (191) and 17% (786) respectively. The prevalence of diagnosed bronchitis was higher in Leipzig than Munich (30.9% (303) *v* 15.9% (739);  $p < 0.01$ ). A significant drop in forced expiratory volume ( $> 9\%$ ) after cold air challenge was measured in 6.4% (57) of children in Leipzig and in 7.7% (345) of those in Munich. Hay fever (2.4% (24) *v* 8.6% (410);  $p < 0.01$ ) and typical symptoms of rhinitis (16.6% (171) *v* 19.7% (961);  $p < 0.05$ ) were reported less often in Leipzig than in Munich.

**Conclusions**—No significant differences were seen in the lifetime prevalence of asthma, wheezing, and bronchial hyperresponsiveness between children in Leipzig and Munich. The lifetime prevalence of bronchitis was higher in Leipzig than in Munich. The lower prevalence rates of allergic disorders in Leipzig could point toward aetiological factors that are associated with Western lifestyle and living conditions.

## Introduction

Morbidity related to asthma has been reported to be increasing in Western countries.<sup>1-5</sup> Rates of death and hospital admission caused by asthma have been rising,<sup>6,9</sup> and prevalence studies in Australia,<sup>4</sup> New Zealand,<sup>5</sup> Switzerland,<sup>1</sup> and Wales<sup>2</sup> have found consistently higher prevalences of asthma and wheezing among children than similar studies 15 to 25 years earlier. Although changes in medical practice, diagnostic labelling, and public awareness could have influenced these trends, Burney *et al* suggested that the increase is real.<sup>3</sup> Similar changes have been reported for the prevalence of hay fever<sup>1,2,10,11</sup> and eczema in children.<sup>1,2,12</sup>

The causes of the apparent increase in the prevalences of asthma and allergic disorders remain unclear. Domestic factors such as exposure to house dust mites,<sup>13</sup> cigarette smoke,<sup>14</sup> or family size<sup>15</sup> have been incriminated, as have environmental factors such as air pollution due to sulphur dioxide, particulate matter, nitrogen dioxide, ozone, or vehicle exhausts.<sup>16-21</sup>

The reunification of Germany provided a unique opportunity to study two genetically similar populations who over the past 45 years have been exposed to different living conditions and levels of environmental pollution. In particular, the type of air pollution differs greatly between western and eastern Germany. The objective of this study was to compare the prevalences of asthma and allergic disorders among children in Munich, western Germany, and Leipzig, eastern Germany, where air concentrations of sulphur dioxide are particularly high. A prevalence survey of 9-11 year old children was carried out in both cities by the same methods.

## Subjects and methods

### STUDY AREAS AND POPULATIONS

Munich is a city with moderate industry and heavy traffic, has a population of about 1.3 million, and is located in southern Bavaria. All fourth grade pupils ( $n=7445$ ) at all primary schools in Munich were included in the study. Leipzig, a city with heavy air pollution caused by private coal burning and industrial emissions, has about 535 000 inhabitants and is located in north west Saxony. All pupils ( $n=1429$ ) attending classes of the fourth grade at a random sample of 28 schools were included in the study.

The study was approved by the ethics committee of the Bavarian Medical Society. We studied children in Munich from September 1989 until July 1990 and those in Leipzig from January 1991 until June 1991.

### QUESTIONNAIRE

A self administered questionnaire was distributed through the schools to the parents of the children. The questionnaire was developed according to international recommendations<sup>22</sup> and included questions concerning sociodemographic characteristics, doctors' diagnoses, typical symptoms of respiratory and allergic disorders, triggers and seasonal patterns of these health problems, therapeutic management, and possible aetiological factors.

Parents were asked: has a doctor ever diagnosed one of the following diseases in your child? (a) asthma, (b) wheezy bronchitis, (c) bronchitis, (d) none of these. In addition, parents were asked whether the condition had occurred only once or more than once. Children whose parents reported either asthma or recurrent wheezy bronchitis were classified as having asthma. Children with reported recurrent bronchitis only were defined as having bronchitis. Additional questions included: has your child ever had wheezing or whistling in the chest? has your child ever had attacks of shortness of breath? does your child cough frequently during the night? does your child cough frequently after exercise or during foggy or cold weather? has a doctor ever diagnosed hay fever in your child? has your child had a runny, stuffy, or itching nose without a cold in the past 12 months? what are the causes of these nose problems? do these symptoms occur during specific months? has a doctor ever diagnosed eczema in your child? has your child ever had itchy rashes in the creases of the knees, elbows, or wrists?

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The Pneumoscope II (Jäger, Würzburg, Germany) was used to test pulmonary function. Forced expiratory manoeuvres were performed and flow volume curves recorded until three reproducible loops were obtained. The highest readings for forced expiratory volume in one second and forced vital capacity during any manoeuvre were used. Cold air hyperventilation was induced with the RHES (respiratory heat exchange system) cold air hyperventilation provocation device (Jäger, Würzburg). Each child did four minutes of isocapnic (5% carbon dioxide) hyperventilation (that is, 22×forced expiratory volume/minute) of dry and cold air (-15°C, at the mouthpiece). Ventilatory effort was guided by a target balloon. The balloon was filled with air at the predetermined rate and had to be kept filling through the respiratory effort of the children. Lung function tests were repeated four minutes after completion of cold air provocation. Only children whose parents had given informed consent participated.

Lung function parameters are expressed as percentages of the predicted value. The 95th centile of the reference population (932 German children without any allergic or respiratory disorders in Munich) was defined as the cut off point.<sup>23</sup> Percentage changes of forced expiratory volume in one second (FEV<sub>1</sub>) after cold air inhalation are calculated as (FEV<sub>1</sub> after inhalation - FEV<sub>1</sub> before inhalation) × 100 / FEV<sub>1</sub> before inhalation.

#### AIR POLLUTION

Information about the air pollution was derived from reports of the responsible local agencies—that is, Bayerisches Landesamt für Umweltschutz in Munich and Landesuntersuchungsanstalt für das Gesundheits- und Veterinärwesen Sachsen in Leipzig. The data for 1989 are presented because they reflect best the long term exposure of children in both areas before the drastic changes occurred in Leipzig following German reunification. The measurement technique for particulate matter (β absorption) was comparable in both areas, and reflects the concentration of particles of less than 30-40 μm. Sulphur dioxide in Leipzig was

measured by a coulometric method. In 1991, however, this method gave results very similar to data obtained by ultraviolet fluorescence, which was recently installed in Leipzig and was also used in Munich. The reported monthly average concentrations of sulphur dioxide and particulate matter in 1989 differed greatly between Leipzig and Munich (fig 1).

No comparable measurements of nitrogen dioxide were available before 1991. The annual average concentrations of nitrogen dioxide in 1991, measured by chemiluminescence, were lower in Leipzig (39 μg/m<sup>3</sup>) than in Munich (58 μg/m<sup>3</sup>). Measurements by the Salzman technique suggest that nitrogen dioxide concentrations in Leipzig have been increasing since 1989. Information about ozone levels is not sufficient to make valid comparisons between the two cities. Measurements recorded in 1991 show annual average concentrations of 39.1 μg/m<sup>3</sup> in Leipzig and of 31.0 μg/m<sup>3</sup> in Munich with maximal half hourly concentrations of 236 μg/m<sup>3</sup> in Leipzig and of 186 μg/m<sup>3</sup> in Munich during the summer. However, no ozone measurements were available for Leipzig before 1991 and the measurement stations in both cities probably underestimate the ozone concentrations for most parts of the city because they are located along busy roads.

#### STATISTICAL METHODS

Based on the prevalence in Munich it was calculated that 1400 children would be needed in Leipzig to detect a difference of 2.5% in the prevalence of asthma with an α error of 5% and a power of 80%. Prevalences were calculated with 95% confidence intervals.<sup>24</sup> Two tailed exact Fisher tests were used to compare prevalence in the two study populations. Prevalence odds ratios were computed as measures of the association between the region and the prevalence of diseases. All calculations were performed with SAS 6.06 software.<sup>25</sup>

#### Results

Parents returned the questionnaire for 1084 (75.8%) children in Leipzig and 6490 (87.0%) in Munich. The proportion of children without German nationality was 3.0% (33) in Leipzig and 22.5% (1460) in Munich. To keep the two study populations as similar as possible with regard to ethnic background the analysis was restricted to children with German nationality. The remaining children in Leipzig and Munich were similar with regard to sex and age distribution, height, and body weight (table I).

The lifetime prevalence of asthma diagnosed by a doctor was slightly lower in Leipzig than in Munich; the lifetime prevalence of wheeze was slightly higher in Leipzig than in Munich (table II). The reported prevalence of nocturnal cough and shortness of breath was similar in both cities, while coughing after exercise or during foggy or cold weather was reported more often in Leipzig than in Munich (18.6% (182) v 11.7% (560); p < 0.05). A significant excess of recurrent bronchitis diagnosed by a doctor was found in Leipzig compared with Munich (30.9% (303) v 15.9% (739); p < 0.01).

Parents of children in whom a doctor had diagnosed asthma in Leipzig and Munich reported wheezing, shortness of breath, nocturnal cough, and cough after exercise with similar frequency (table III). Parents of children with a doctor's diagnosis of bronchitis without asthma reported cough following exercise or during cold or foggy weather more often in Leipzig than in Munich (27.9% (78) v 19.0% (133); p < 0.01). No significant differences between Leipzig and Munich were found for the reported frequency of wheezing, attacks of shortness of breath, and nocturnal cough among children with bronchitis.

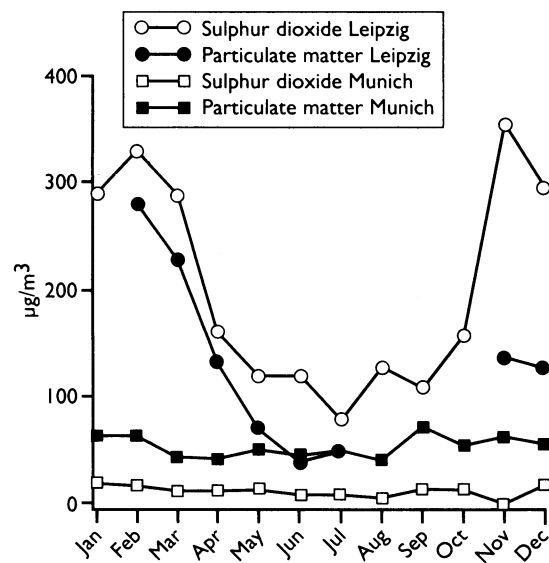


FIG 1—Average monthly concentration of sulphur dioxide and particulate matter in Munich and Leipzig in 1989. Measurements of particulate matter in Leipzig were not available for January, August, September, and October

TABLE I—Mean (95% confidence interval) age, height, and body weight of the study of children in Leipzig and Munich

	Leipzig (n=1051)		Munich (n=5030)	
	Boys (n=491)	Girls (n=560)	Boys (n=2445)	Girls (n=2585)
Age (years)	9.92 (9.88 to 9.96)	9.91 (9.87 to 9.95)	9.82 (9.80 to 9.84)	9.75 (9.73 to 9.77)
Height (cm)	143.2 (142.6 to 143.8)	143.8 (143.3 to 144.4)	143.5 (143.2 to 143.7)	142.9 (142.6 to 143.2)
Weight (kg)	34.9 (34.3 to 35.5)	35.3 (34.7 to 35.8)	34.8 (34.5 to 35.0)	34.4 (34.1 to 34.6)

Table IV shows the reported triggers of asthma attacks for both study populations. Colds and foggy weather were most often incriminated in Leipzig while grass pollen and dust and emotional problems were reported most often as triggers by parents in Munich.

The prevalence of hay fever diagnosed by a doctor was significantly lower in Leipzig than in Munich (2.4% (24) v 8.6% (410);  $p < 0.01$ ) (table II). Typical symptoms of rhinitis—runny, stuffy, or itching nose—during the previous 12 months were also reported less often in Leipzig than in Munich (16.6% (171) v 19.7% (961);  $p < 0.05$ ). Allergic triggers of rhinitis symptoms such as grass, pets, or dust were reported also less often

TABLE II—Lifetime prevalence (%) of respiratory and allergic disorders among 9-11 year old children in Leipzig and Munich

	Leipzig (n=1051)		Munich (n=5030)		Odds ratio (95% confidence interval)
	No of children	Prevalence (95% confidence interval)	No of children	Prevalence (95% confidence interval)	
Doctor diagnosed:					
Asthma	72	7.3 (5.7 to 9.0)	435	9.3 (8.5 to 10.2)	0.77 (0.59 to 1.00)
Bronchitis	303	30.9 (26.0 to 33.8)	739	15.9 (14.8 to 16.9)	2.37 (2.03 to 2.77)**
Hay fever	24	2.4 (1.4 to 3.3)	410	8.6 (7.8 to 9.4)	0.26 (0.17 to 0.39)**
Atopic dermatitis	129	13.0 (10.9 to 15.1)	667	13.9 (12.9 to 14.9)	0.93 (0.76 to 1.13)
Reported symptoms:					
Wheeze	191	20.0 (17.4 to 22.5)	786	17.0 (15.9 to 18.1)	1.22 (1.02 to 1.45)
Attacks of shortness of breath	73	7.3 (5.7 to 8.9)	416	8.7 (7.9 to 9.5)	0.83 (0.64 to 1.08)
Nocturnal cough	34	3.4 (2.2 to 4.5)	166	3.4 (2.9 to 3.9)	0.98 (0.67 to 1.43)
Cough after exercise or during foggy or cold weather	182	18.6 (16.1 to 21.0)	560	11.7 (10.8 to 12.6)	1.72 (1.43 to 2.04)**
Runny, stuffy, or itching nose in past 12 months	171	16.6 (14.4 to 18.9)	961	19.7 (18.6 to 20.8)	0.81 (0.68 to 0.97)*
Itchy skin, rashes	184	18.1 (15.7 to 20.4)	862	17.7 (16.7 to 18.8)	1.02 (0.86 to 1.22)

\* $p < 0.05$ , \*\* $p < 0.01$  calculated with Fisher's two tailed exact test.

TABLE III—Prevalence (%) of respiratory symptoms in children with diagnosed asthma and diagnosed bronchitis in Leipzig and Munich

	Leipzig		Munich		Odds ratio (95% confidence interval)
	No of children	Prevalence (95% confidence interval)	No of children	Prevalence (95% confidence interval)	
Children with asthma:					
Wheeze	72	76.1 (65.9 to 86.3)	435	73.1 (68.8 to 77.5)	1.18 (0.64 to 2.13)
Attacks of shortness of breath	34	49.3 (37.5 to 61.1)	191	46.7 (41.9 to 51.5)	1.11 (0.67 to 1.85)
Nocturnal cough	16	22.5 (12.8 to 32.3)	76	18.4 (14.6 to 22.1)	1.30 (0.70 to 2.38)
Cough after exercise or during foggy or cold weather	36	55.4 (43.3 to 67.5)	187	45.7 (40.9 to 50.5)	1.47 (0.87 to 2.50)
Children with bronchitis:	303		739		
Wheeze	84	30.7 (25.2 to 36.1)	200	29.9 (26.5 to 33.4)	1.04 (0.76 to 1.40)
Attacks of shortness of breath	23	8.1 (4.9 to 11.3)	79	11.4 (9.1 to 13.8)	0.67 (0.42 to 1.12)
Nocturnal cough	14	4.8 (2.3 to 7.2)	32	4.4 (2.9 to 5.9)	1.07 (0.57 to 2.04)
Cough after exercise or during foggy or cold weather	78	27.9 (22.6 to 33.1)	133	19.0 (16.1 to 21.9)	1.64 (1.19 to 2.27)**

\* $p < 0.05$ , \*\* $p < 0.01$  by Fisher's two tailed exact test.

TABLE IV—Reported triggers of symptoms among 9-11 year old children with asthma and symptoms of rhinitis in Leipzig and Munich

	Leipzig		Munich		Odds ratio (95% Confidence interval)
	No of children	% (95% Confidence interval)	No of children	% (95% Confidence interval)	
Children with asthma:					
Colds	68	80.9 (71.5 to 90.2)	406	66.5 (61.9 to 71.1)	2.13 (1.12 to 4.00)
Foggy weather	34	50.0 (38.1 to 61.9)	145	35.7 (31.0 to 40.4)	1.79 (1.08 to 3.03)*
Exercise	16	23.5 (13.4 to 33.6)	103	25.4 (21.1 to 29.6)	0.90 (0.50 to 1.67)
Pets	10	14.7 (6.3 to 23.1)	84	20.7 (16.7 to 24.6)	0.66 (0.32 to 1.35)
Grass	12	17.7 (8.6 to 26.7)	126	31.0 (26.5 to 35.5)	0.48 (0.25 to 0.92)*
Dust	10	14.7 (6.3 to 23.1)	100	24.6 (20.4 to 28.8)	0.53 (0.26 to 1.08)
Emotion	6	8.8 (2.1 to 15.6)	90	22.2 (18.1 to 26.2)	0.34 (0.14 to 0.81)**
Children with symptoms of rhinitis:	150		860		
Pets	7	4.7 (1.3 to 8.0)	104	12.1 (9.9 to 14.3)	0.36 (0.16 to 0.78)*
Grass	23	15.3 (9.56 to 21.1)	336	39.1 (35.8 to 42.3)	0.28 (0.18 to 0.45)*
Dust	13	8.7 (4.2 to 13.2)	143	16.6 (14.1 to 19.1)	0.48 (0.26 to 0.86)*

\* $p < 0.05$ , \*\* $p < 0.01$  by the two tailed exact Fisher test.

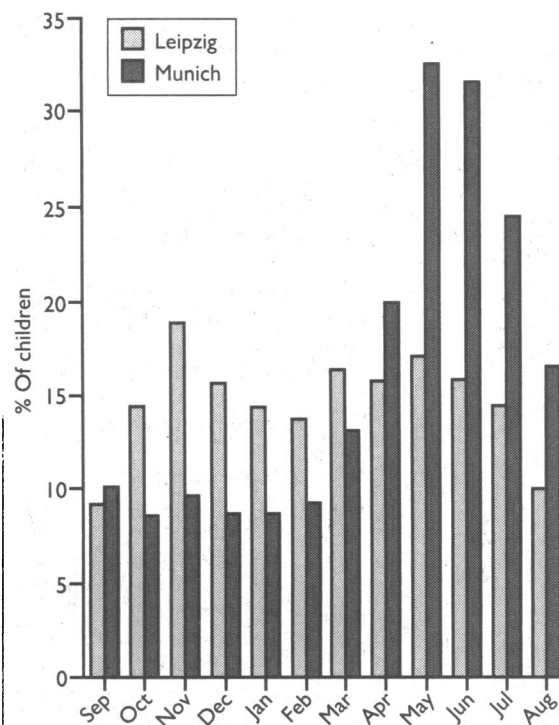


FIG 2—Proportion of children with rhinitis whose parents reported that symptoms occurred during specific months in Leipzig (n=154) and Munich (n=872)

by parents from Leipzig than from Munich (table IV). Parents were also asked to indicate whether symptoms occurred during specific months. In Munich symptoms of rhinitis showed a strong peak during the summer months when pollen counts are high whereas in Leipzig the reported frequency of these symptoms increased only slightly during the summer and also increased during the winter months (fig 2). Atopic dermatitis diagnosed by a doctor and typical symptoms of atopic dermatitis were reported with similar frequency in the two study areas.

Of the eligible children for whom the questionnaire was returned, 889 (95.1%) from Leipzig and 4478 (89%) from Munich participated in the lung function tests. The participating children in Leipzig and Munich were similar with regard to age, sex, height, and body weight. Baseline measures in Leipzig and Munich were 93.1% v 98.3% of predicted for forced vital capacity and 96.0% v 97.5% of predicted for forced expiratory volume in one second. A significant drop in forced expiratory volume (more than 9%) was measured in 6.4% (57) of the children in Leipzig and in 7.7% (345) of the children in Munich (prevalence odds ratio=0.81; 95% confidence interval 0.61 to 1.07).

## Discussion

Our results indicate no large differences in the lifetime prevalence of asthma, wheezing, and bronchial hyperreactivity among children living in Leipzig and Munich. The prevalence of bronchitis and cough after exercise as well as during foggy or cold weather was higher in Leipzig than in Munich. Allergic triggers of asthma and allergic rhinitis were less common in Leipzig than in Munich.

### METHODOLOGICAL PROBLEMS

There may be some methodological limitations. The survey in Leipzig was conducted one year after the Munich study and in only a cluster sample of children. It is unlikely, however, that these differences had a major influence on the study results. Questions concerning the lifetime prevalence are obviously subject to recall bias, which could have operated differently in



the two populations. Until recently people in Leipzig and Munich have lived in a different social and political environment which could have influenced their attitude towards physical complaints as well as their responses to the questionnaire.

Differences in the observed prevalence of doctor diagnosed asthma and bronchitis could be a reflection of different medical practice and diagnostic labelling in the formerly separated states.<sup>20</sup> It is possible that some of the children with bronchitis in Leipzig would have had asthma diagnosed if they were in Munich. Parents of children with bronchitis, however, reported wheezing, attacks of shortness of breath, and nocturnal cough with similar frequency in both cities. Cough after exercise or during foggy or cold weather was reported more often by parents of children with bronchitis in Leipzig. The results of the cold air challenge provide further evidence for a similar prevalence of asthma in Leipzig and Munich. It is unlikely that the increased reporting in Leipzig is strictly a diagnostic bias, even though different diagnostic labelling in the two cities cannot be fully excluded.

The prevalence of medically diagnosed hay fever, the most common form of allergic rhinitis, was much lower in Leipzig than in Munich. Differences in diagnostic labelling between the two cities could have influenced our findings. Nevertheless, not only were typical symptoms of rhinitis less common in Leipzig than in Munich, but parents in Munich also indicated allergic triggers and the typical seasonal pattern of rhinitis symptoms more often than those in Leipzig.

#### AIR POLLUTION

High levels of sulphur dioxide and particulate matter in the air have long been associated with respiratory illness in children and adults.<sup>27-28</sup> A study of schoolchildren in Sheffield found increased rates of respiratory illness among children living in areas with high pollution from sulphur dioxide ( $275 \mu\text{g}/\text{m}^3$ ) and particulate matter ( $301 \mu\text{g}/\text{m}^3$ ).<sup>29</sup> A follow up study of these children four years later, after the introduction of a clean air programme, found big reductions in air concentrations of particulate matters and a fall in respiratory disease among the schoolchildren; concentrations of sulphur dioxide had decreased only slightly during this time.<sup>28</sup> The individual contribution of both compounds of air pollution has since been debated.<sup>30-31</sup>

An increased prevalence of cough has been observed among children intermittently exposed to high concentrations of sulphur dioxide ( $> 2500 \mu\text{g}/\text{m}^3$ ) at moderate levels of particulate sulphates.<sup>30</sup> Experimental studies suggest that sulphur dioxide can increase airway resistance in subjects with pre-existing asthma but not in healthy subjects.<sup>32-34</sup> The American six cities study reported a positive correlation between the prevalence of bronchitis and chronic cough and exposure to particulate matter.<sup>19-31</sup> The odds of bronchitis and chronic cough increased by 2.3 and 3.4 respectively over the range of the observed concentrations ( $34.1-80.0 \mu\text{g}/\text{m}^3$ ) of total suspended particulates and the increase was statistically significant for the concentrations of particulate matter less than  $15 \mu\text{m}$  diameter.<sup>31</sup> However, no association between exposure to particulate matter, nitrogen dioxide, or sulphur dioxide and the prevalence of persistent wheeze or asthma was observed.<sup>19-31</sup> Braun-Fahrländer and colleagues reported a correlation of levels of total suspended particulates with the incidence and duration of episodes of respiratory symptom among preschool children,<sup>30</sup> while others observed an association of levels of particulate matter less than  $10 \mu\text{m}$  with hospital admission rates from respiratory illness.<sup>35</sup>

Our findings of an increased prevalence of bronchitis and frequent cough in Leipzig, which has higher levels of sulphur dioxide and particulate matter than Munich,

confirm earlier reports of this association,<sup>18-20, 29-31</sup> although the relative effects of both pollutants cannot be determined. In turn, the similar prevalence of asthma and bronchial hyperresponsiveness to cold air inhalation in both cities provides additional evidence<sup>19-29, 30</sup> that long term exposure to sulphur dioxide and particulate matter, even at the observed high levels, does not primarily affect bronchial hyperresponsiveness and asthma.

#### POPULATION DIFFERENCES

Children in Munich are exposed to higher concentrations of nitrogen dioxide than those in Leipzig, which probably reflects the higher concentrations of automobile exhausts caused by heavy traffic in Munich. Diesel exhausts have been reported to have an adjuvant effect on allergic sensitisation in animal models<sup>36</sup> and another study from Japan suggests that pollution from automobile exhaust in areas with high pollen counts may increase the incidence of hay fever in humans.<sup>16</sup> Exposure to nitrogen dioxide and auto-mobile exhaust might be partly responsible for the higher prevalence of allergic rhinitis in Munich.

Not only air pollution but living conditions in the two cities have been very different over the past 45 years. Relevant differences between living conditions in Leipzig and Munich might include nutrition, parental smoking habits, housing conditions, and respiratory infections early in life. Our study based on only two centres does not allow us to attribute disease differentials to specific causes. We aimed at giving a descriptive comparison of the prevalence of asthma and allergic disorders among children living in western and eastern Germany. Further studies are currently underway to address aetiological questions in more detail. The apparently lower prevalence of allergic disorders in Leipzig was particularly interesting. These findings could point toward aetiological factors for allergic disease that are associated with the lifestyle and living conditions in Western industrialised countries.

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## Medical management of missed abortion and anembryonic pregnancy

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Miscarriage is the most common complication of pregnancy and probably accounts for around 50 000 inpatient admissions in the United Kingdom each year. Generally, its management has changed little with time. Recently developments in non-surgical treatment, refined in induced abortion, offer an opportunity to improve management and to remove the need for surgery and anaesthesia. We report our initial experience of the use of mifepristone (an antiprogesterone) and misoprostol (a synthetic analogue of prostaglandin E<sub>1</sub>) in the management of missed abortion and anembryonic pregnancy (gestation sac present but no developing embryo).

### Patients, methods, and results

Sixty women with a diagnosis of missed abortion or anembryonic pregnancy equivalent to 13 weeks' gestation or less were recruited after counselling. Twenty five of the women had been referred for ultrasound scanning because of bleeding in early pregnancy, while in the remainder the diagnosis had been made on routine scanning when they booked. Patients in whom an incomplete abortion was diagnosed were not included.

Each patient was given a single oral dose of mifepristone 600 mg and was admitted to the gynaecological ward as an outpatient 36-48 hours later, when misoprostol 600 µg was given orally in a divided dose (400 µg and, two hours later, 200 µg). The patient's pulse, blood pressure, and temperature were recorded hourly, as were any side effects and requests for analgesia. If the products of conception were not expelled and verified within four hours vaginal ultrasonography was performed. If the gestation sac was not seen and bleeding had occurred the procedure was considered to have been successful, but if not the patient was offered evacuation of the uterus under general anaesthesia. All patients were reviewed 10-14 days later.

The median age of the 60 women was 27 (range 15-44), and the median duration of amenorrhoea was 71 (42-110) days. Twenty nine patients were diagnosed as having anembryonic pregnancies and the remaining 31 as having had a missed abortion. One of the patients thought to have an anembryonic pregnancy was

eventually found to have an ectopic pregnancy when she failed to abort. She has been excluded from further consideration.

Eight patients aborted with mifepristone alone. Of the 51 remaining patients, 43 aborted after taking misoprostol 600 µg and five more aborted after receiving a second divided dose of 600 µg misoprostol. In three patients the treatment failed, and they underwent evacuation of the uterus under general anaesthesia. Exploratory curettage was performed in two other patients at 14 and 22 days after treatment with misoprostol, but no products of conception were obtained.

The median time from administration of misoprostol to abortion was 4 (range 1-11) hours. The median duration of bleeding after abortion was 10 (2-22) days. There were no cases of infection, and no patient required antibiotic treatment. Side effects from misoprostol treatment (nausea, vomiting, and diarrhoea) were few: antiemetic drugs were given to five patients, and diarrhoea was reported by seven. Thirty nine women did not ask for any pain relief, 13 requested oral analgesia, and seven required parenteral analgesia.

### Comment

The medical management of induced abortion is now established practice, and several centres have developed considerable skill in using mifepristone with a variety of prostaglandin analogues.<sup>1-4</sup> We have shown the clinical feasibility of managing missed abortion and anembryonic pregnancy medically without resort to surgery or anaesthesia. Patients' perceptions at this early stage of development of the method are positive but need to be assessed more thoroughly, particularly in relation to the alternatives. The implications in terms of resources are considerable since if this method became standard practice a major part of emergency work in gynaecology would be removed from the operating room and could be managed at times more convenient to patients and staff.

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