335

# Papers and Originals

## Observations on Recent Increase in Mortality from Asthma

F. E. SPEIZER,\* M.D.,; R. DOLL, M.D., F.R.C.P., F.R.S.; P. HEAF, M.D., F.R.C.P.

Brit. med. J., 1968, 1, 335-339

An increase in the mortality from asthma, particularly in children, has been reported from Australia (Gandevia, 1967). the United States (Richards and Patrick, 1965), and Britain (Smith, 1966), and suggestions have been made that the increase is due to the introduction of new methods of treatment (Ford, 1966; Kessler and Geller-Bernstein, 1966; Greenberg and Pines, 1967). We have therefore examined the trends in mortality from asthma throughout the world and have sought evidence to account for the increase in England and Wales.

### Trends in Mortality at All Ages

Before 1948 deaths classified as asthma ranged from various forms of bronchitis and influenza to deaths associated with a variety of cardiovascular, renal, and allergic diseases. In 1948, with the sixth revision of the International Classification of Diseases, asthma was given a more specific category (List No. 241), but it was still classified with several conditions in which asthma may have played only a subsidiary part. These included "asthmatic bronchitis" and other forms of bronchitis where asthma was mentioned without specifying that it was allergic. When the seventh revision of the Classification was undertaken in 1955 these types of "bronchitis" were removed and the asthma category began to correspond to a single disease entity (Table I).

These changes reflect, in part, changes in the clinical concept of the disease, and further revisions may be expected as diagnostic precision and knowledge of causation improve. Meanwhile the available statistics can be used only as initial guides to trends in mortality.

TABLE I.—International Classification of Causes of Death: Description of Deaths Attributed to Asthma Between 1938 and 1966

	1938-1947—5th Re	evision of I.C.D.
112 A	sthma	•
	Asthmatic bronchitis	Hay asthma
	Bronchial asthma	Hay fever
	Bronchitic asthma	Spasmodic asthma
	Catarrhal asthma	-
112.1	With influenza as a contribution	
112.2	With chronic endocarditis	as a contributory or
	secondary cause	
112.3	With myocardial disease	as a contributory or
	secondary cause	
112.4	With arteriosclerosis as a co	ontributory or secondary
	cause	
112.5	With chronic nephritis	as a contributory or
	secondary cause	
112.6	Without any of the compli-	cations here specified (1–5

1948-1957-6th Revision of I.C.D. Asthma (bronchial) Allergic (any cause)
Sporadic
Asthmatic bronchitis
Hay fever with asthma
This title excludes cardiac asthma (434.2) and pneumoconiotic asthma (523–524) Bronchitis, allergic -7th Revision of L.C.D.

241 Asthma (bronchial)
Allergic (any cause)
Sporadic

Bronchitis, allergic

Sporadic Hay asthma
Hay fever with asthma
This title excludes cardiac asthma (434.2) and pneumoconiotic asthma (523-524.)
It also excludes asthma not indicated as allergic with mention of bronchitis (acute) (chronic) (500-502).

In England and Wales the number of deaths decreased progressively from 1,879 in 1952 to 1,507 in 1957, dropped with the new classification to 1,214 in 1959, and rose subsequently to 2,040 in 1966. Between 1959 and 1966 the death rate increased by 56%, from 2.7 to 4.2 per 100,000 persons.

The trends in 19 countries between 1951 and 1964 have been summarized by the World Health Organization (1966). These

- (1) In virtually every country there was a sharp decline in the crude mortality rate between 1957 and 1959 which presumably reflected the change from use of the sixth revision of the International Classification to the seventh revision.
- (2) With the exception of Venezuela, every country with data available before 1958 showed an excess mortality in males, and since 1958 this excess has been reduced. Before 1958 the excess is likely to have been due to the inclusion of a high proportion of deaths from bronchitis, a condition which is appreciably commoner in males.
- (3) In 1964 the crude mortality varied between the countries from 1.1 to 9.7 per 100,000 persons, a variation which is likely to be due, in part, to variation in diagnostic criteria.
- (4) Between 1959 and 1964 several countries showed sporadic increases in mortality, but the general picture is of a constant rate with a slight tendency to decrease.
  - (5) England and Wales alone showed a steady increase.

#### Trends in Age-specific Mortality

Not all the deaths attributed to asthma are likely to have been due to asthma, and this is particularly true for deaths that occurred in infancy and old age. Under 5 years of age asthma may be confused with bronchiolitis or bronchitis which has led to airway obstruction and presented as overinflation with wheezing. Over 65 years of age asthma is commonly complicated by bronchitis and heart failure, which may be the result of the underlying respiratory disease or of independent heart disease. In both these age groups the selection of asthma as the underlying cause of death is partly subjective, and many deaths attributed to asthma could more properly be attributed to other causes.

A more accurate picture of the trend in mortality attributable to the disease may therefore be obtained by confining the comparison to ages 5 to 64 years. At these ages the increase in mortality in England and Wales is even more pronounced; the annual number of deaths increased from 720 in 1959 to 1,401 in 1966, and the corresponding death rate nearly doubled (from 2.0 to 3.7 per 100,000 persons).

\* U.S. Public Health Service Special Fellow, Medical Research Council's

Statistical Research Unit.
† Director, Medical Research Council's Statistical Research Unit.
‡ Chest Physician, University College Hospital, London W.C.1.
Requests for reprints should be addressed to Dr. R. Doll, University College Hospital Medical School, 115 Gower Street, London W.C.1.

Figs. 1 and 2 show that the rates have been approximately equal in both sexes in three age groups—10 to 14 years, 5 to 34 years, and 35 to 64 years. Between 1957 and 1960 the rates fell at ages 35 to 64 years, due largely to the change in the method of classification, but there was little consistent change at younger ages. Since 1960–61 the rates have increased.

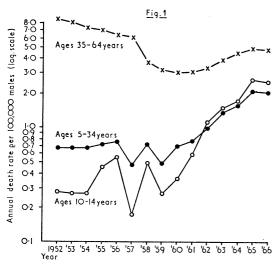


Fig. 1.—Asthma mortality in males aged 10 to 14 years, 5 to 34 years, and 35 to 64 years in England and Wales from 1952 to 1966.

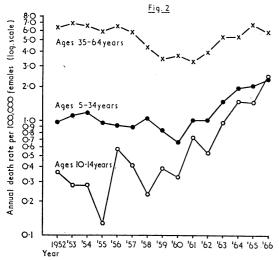


Fig. 2.—Asthma mortality in females aged 10 to 14 years, 5 to 34 years, and 35 to 64 years in England and Wales from 1952 to 1966.

Table II shows the changes since 1959 in greater detail. Since the male and female rates have been approximately equal the figures for both sexes have been combined to reduce the effect of random fluctuation due to small numbers. From Table II it is evident that an increase in mortality began to occur in about 1961 and that all ages between 5 and 64 years of age have been affected. The greatest increase in mortality has taken place at ages 10 to 14 years, at which ages the rate has increased eight times, from 0.3 to 2.5 per 100,000 persons. The increase has, however, been substantial at all ages from 5 to 34 years, and at these ages the annual number of deaths increased by 308 and the death rate trebled from 0.7 to 2.2 per 100,000 persons.

In the rest of this paper we have confined our observations to mortality at ages 5 to 34 years, partly because this age group has shown a large increase in mortality, partly because asthma which develops under 35 years of age is usually classed as

"allergic" and can be distinguished clinically from the disease which develops at a later age, and partly because the mortality from bronchitis begins to exceed that from asthma at about 35 years of age and the possibility of confusing these conditions as the cause of death increases rapidly with advancing years.

TABLE II.—Number of Deaths and Death Rates from Asthma per 100,000 Persons, by Age: England and Wales, 1959 to 1966\*

Age in Years	Deaths	1959	1960	1961	1962	1963	1964	1965	1966
5-9 {	No.	6	12	6	6	9	23	18	17
	Rate	0·18	0·37	0·18	0·18	0·27	0·67	0·51	0·47
10-14	No.	12	13	24	29	41	53	66	80
	Rate	0·33	0·35	0·65	0·84	1·21	1·60	2·02	2·46
15-19	No.	19	17	24	39	36	62	73	91
	Rate	0·64	0·55	0·77	1·11	0.99	1·67	1·96	2·45
20-24{	No.	24	27	28	32	56	51	79	83
	Rate	0·85	0·94	0·97	1·09	1·87	1·66	2·49	2·52
25-29{	No.	32	28	39	38	45	69	90	79
	Rate	1·12	0·98	1·37	1·31	1·53	2·33	3·00	2·64
30-34	No.	30	31	48	47	83	84	77	81
	Rate	0.99	1·04	1·61	1·57	2·79	2·85	2·63	2·78
5-34	No.	123	128	169	191	270	342	403	431
	Rate	0·66	0·68	0·89	1·00	1·40	1·76	2·05	2·18
35-64	No.	597	594	568	655	845	903	1,072	970
	Rate	3·32	3·29	3·13	3·60	4·64	4·96	5·89	5·34
5–64	No.	720	722	737	846	1,115	1,245	1,475	1,401
	Rate	1·96	1·96	1·99	2·26	2·97	3·30	3·90	3·69
All ages {	No.	1,214	1,188	1,269	1,352	1,655	1,800	2,080	2,040
	Rate	2·67	2·60	2·75	2·89	3·52	3·80	4·35	4·24

<sup>\*</sup> From the Registrar General's Statistical Reviews of England and Wales for 1959 to 1965, the Quarterly Return for England and Wales, 3rd Quarter 1966, and personal communication.

The relative importance of the increase in mortality between 1959 and 1966 is indicated by the change in the proportion of all deaths attributed to asthma over the same period. In 1959 and 1960 approximately 1% of all deaths at ages 5 to 34 years were attributed to asthma; in 1966 the proportion was 3.4%. At ages 10 to 14 years the proportional mortality increased from 1% to 7.2%.

Data are not yet available for the numbers of deaths due to other causes in 1966; but in 1965, when asthma accounted for 5.7% of all deaths at ages 10 to 14 years, it ranked sixth in the list of causes of death (Table III). The only categories with

TABLE III.—Ten Major Causes of Death in England and Wales in Children Aged 10-14 Years for the Year 1965\*

6 (D.1.((CD)	N	0.	Total	Percentage of Total Deaths	
Cause of Death (I.C.D.)	Male	Female	Total	in Age Group	
All motor accidents (E810- E825)	127	66	193	16-6	
than leukaemia (I.C.D. 140-203, 205) 3. All congenital malformations	85	39	124	10.7	
(I.C.D. 750–759)	50	51	101	8.7	
4. All diseases of nervous system (I.C.D. 330-398) 5. Leukaemia and aleukaemia	53	37	90	7.8	
(I.C.D. 204) 6. Asthma (I.C.D. 241)	39 <b>4</b> 3	35 23	74 66	6·4 5·7	
7. All pneumonia ( <i>I.C.D.</i> 490–493) 8. Drowning (E929)	27 44	36 9	63 53	5·4 4·6	
9. All gastrointestinal diseases (I.C.D. 530-587)  10. All genito-urinary diseases	31	19	50	4.3	
(I.C.D. 590–637)	14	33	47	4.1	
All other diseases	190	109	299	25.8	
Total all diseases	703	457	1,160	100.0	

<sup>\*</sup> Registrar General's Statistical Review of England and Wales for the Year 1965.

substantially higher rates were motor accidents (I.C.D. List Nos. E810 to E825), malignant neoplasms other than leukaemia (List Nos. 140–203, 205), congenital malformations (List Nos. 750–759), and diseases of the nervous system and sense organs (List Nos. 330–398). Other diseases whose rates were of the same order as asthma were leukaemia (List No. 204) and pneumonia (List Nos. 490–493).

#### Trends in Other Countries

Mortality rates and trends in mortality in other countries fall into two fairly distinct groups. Those countries whose death rate for asthma at ages 5 to 34 was less than 0.5 per 100,000 persons in 1959 to 1960 and those whose rate ranged between 0.5 and 1 per 100,000 persons. The United States and virtually all western European countries apart from Britain (including Belgium, France, Italy, Netherlands, Spain, West Germany, Denmark, and Sweden) fall into the first group, and none of these showed any appreciable increase in mortality up to 1964, irrespective of whether or not they showed any change in total asthma mortality at all ages.

The remaining countries need to be considered individually. Scotland's death rate for asthma at ages 5 to 34 years was generally lower than in England and Wales. After 1962, however, the increase in the number of deaths was similar. The increase became appreciable in 1963, and in 1964 the rate was approximately three times the average for 1961 and 1962. At ages 35 to 64 years there has also been some increase, but less pronounced.

Before 1964 Australian death rates at ages 5 to 34 years were higher than in England and Wales; and until then they were relatively stable. A substantial increase took place from 1963 to 1964 (from 0.9 to 1.8 per 100,000 persons), but there was no further increase in 1965. In contrast to England and Wales and Scotland, comparable increases also occurred at ages 10 to 14 years and at ages 35 to 64 years.

In Japan the rates have shown a somewhat different trend. At ages 5 to 34 years there has been a steady but rather slow increase in mortality, which in 1964 had risen by about 40%, in contrast to the rise of over 250% in England and Wales. This, however, was accompanied by a decrease in mortality at ages 35 to 64 years.

New Zealand alone had an asthma death rate at ages 5 to 34 years of over 0.5 per 100,000 persons in 1959 and showed no increase in mortality in the next six years.

Different results are obtained when the comparison is limited to ages 10 to 19 years—the decade in which the largest increase was recorded in England and Wales. Five-year age-specific rates are available for the whole period 1959 to 1964 for only 11 countries, and these are shown in Table IV. The individual

TABLE IV.—International Death Rates from Asthma for Ages 10-14 and 15-19 Years: 1959-61 and 1962-4\*

1) consequent of the first interest of the state delensation of the state of the st		195	9–1961	196	Per		
Country	Age in Years	No. of Deaths	Average Yearly Death Rate per 100,000	No. of Deaths	Average Yearly Death Rate per 100,000		
Britain: England and Wales Scotland	} 10-14	59	0·48	143	1·26	162·5	
	15-19	69	0·67	151	1·23	83·6	
Australasia: Australia† New Zealand	} 10-14 15-19	21 30	0·56 0·94	44 40	1·14 1·16	103·6 23·4	
Europe: Germany Sweden Denmark Netherlands Belgium Japan	10-14	29	0·21	54	0·39	85·7	
	15-19	31	0·24	47	0·35	45·8	
	10-14	87	0·26	147	0·50	92·3	
U.S.A	15-19	107	0·38	172	0·55	44·7	
	10-14	104	0·21	140	0·26	23·8	
	15-19	124	0·30	153	0·33	10·0	

<sup>•</sup> Data compiled from the Official National Vital Statistics Record for each country for the years 1959-1964, with the exception of Australia.
† Data from Dr. B. Gandevia (personal communication).

results are irregular, but when the countries are grouped regionally, to reduce the effect of random fluctuation of small numbers, it is found that there has been an increase in mortality rates from 1959-61 to 1962-4 in each region. The increase has been largest in Britain—162% at ages 10 to 14 years and 84%

at ages 15 to 19 years. In Western Europe, Japan, and Australasia increases have occurred in the range of 85 to 103% at ages 10 to 14 years and in the range of 23 to 45% at ages 15 to 19 years. In the United States the increases have been small, but they still show the same trend. Small increases were again observed in 1965 (to 0.30 and 0.40 per 100,000), but provisional data for 1966, for which we are indebted to the Division of Vital Statistics of the Department of Health, Education, and Welfare of the U.S. Public Health Service, suggest that a substantial increase may now have occurred. From 1965 to 1966 the number of deaths attributed to asthma at ages 1 to 14 years increased by 64%, from 146 to 240.

#### Reasons for Increased Death Rate

One possible explanation of the increase in England and Wales is that it is an artifact brought about by changes in the diagnostic criteria used by physicians certifying the cause of death. This possibility has been investigated by comparing the trends in mortality attributed to asthma and a variety of other respiratory diseases; that is, from all forms of bronchitis (I.C.D. List Nos. 500-502), bronchiectasis (List No. 526), emphysema without mention of bronchitis (List No. 527.1, pneumonia (List Nos. 490-493), and other chronic interstitial pneumonias (List No. 525). The annual numbers of deaths and the death rates attributed to these causes are summarized in Table 5. Some decrease occurred in the number of deaths attributed to pneumonia, but the reduction (107 deaths between 1959 and 1965) is less than a half of the increase in asthma deaths (280 over the same period) and the pneumonia death rate oscillated while the asthma mortality increased steadily. No appreciable change took place in the death rates attributed to bronchitis or other chronic respiratory diseases, and changes in the use of these categories cannot by themselves have led to an increase in the number of deaths attributed to asthma. Moreover, the number of deaths attributed to bronchitis for which asthma was mentioned on the death certificate did not decrease at these ages—as would be expected if there had been a tendency for doctors to attribute the underlying cause to asthma alone rather than to asthma and bronchitis-but increased from 24 in 1959 to 49 in 1966.

TABLE V.—Death Rate per 100,000 Persons Aged 5-34 Years from Selected Respiratory Diseases: England and Wales 1959-1965\*

Diagnostic Category	Deaths	1959	1960	1961	1962	1963	1964	1965
Acute and chronic bronchitis (I.C.D. 500-502)	No.	121	107	124	128	126	121	131
	Rate	0·65	0·57	0·66	0·67	0·65	0·62	0·66
Chronic respiratory† diseases ( <i>I.C.D.</i> 525, 526, 527.1)	No.	84	92	73	76	73	76	78
	Rate	0·45	0·49	0·39	0·40	0·38	0·39	0·40
Pneumonias (I.C.D. 490–493) {	No.	486	403	423	474	416	398	379
	Rate	2·61	2·15	2·24	2·47	2·15	2·04	1·93
Asthma (I.C.D. 241)	No.	123	128	169	191	270	342	403
	Rate	0·66	0·68	0·89	1·00	1·40	1·76	2·05

<sup>\*</sup> From the Registrar General's Statistical Review of England and Wales for each year 1959-1965.
† See text for definition.

Further evidence is provided by the fact that the number of asthma deaths that were certified by coroners after necropsy examination increased even more rapidly than the total (from 43 at ages 5 to 34 years in 1959 to 237 in 1966). If the increase were an artifact we should have to postulate that there had been an even greater change in the diagnostic criteria used by pathologists than in those used by clinicians, or that there had been a change in the type of case referred to coroners.

We conclude, therefore, that the increase in mortality attributed to asthma at ages 5 to 34 years is, in large part, real and represents a true increase in the annual number of deaths from the disease.

#### Two Explanations

One explanation of a true increase in mortality could be that the number of patients suffering from asthma had risen. This cannot be tested directly, but an indication of its validity can be obtained by comparing the frequency with which patients have consulted their general practitioners. In 1955 to 1956 the Royal College of General Practitioners in co-operation with the Registrar General collected figures on morbidity from a variety of diseases, including asthma (Fry, 1962), and similar data have been made available to us for the years 1961 to 1966 for a selected group of practices covering approximately 20,000 patients (Table VI). Over this 10-year period there has, in fact, been a tendency for the number of episodes of asthma leading to consultation to decrease at ages 5 to 14 years and to stay approximately the same at ages 15 to 44 years. A reduction in the number of episodes at young ages could be due to a decrease in the incidence of the disease or to some change in therapy keeping the patients away from the doctor; but even in the latter case it would seem most unlikely that the incidence of the disease could have increased appreciably.

TABLE VI.—Morbidity from Asthma Recorded in General Practice

Episodes per Year per 1,000 Persons Aged (in Years):	1955-6*	1961†	1962	1963	1964	1965	1966
5-14 15-44 45-65	10 7 10	9·2 6·6 5·2	4·9 3·6 9·3	6·8 3·0 5·1	3·9 5·1 5·2	4·9 6·4 4·5	4·3 6·6 9·6
All ages	9	5.8	3.8	5.6	5.2	5.3	4.6

\* Fry (1962). † 1961 to 1966, Dr. D. L. Crombie, Royal College of General Practitioners (personal communication).

Another explanation could be that there has been an increase in the case fatality rate. We have again not been able to test this directly, but it is notable that the proportion of asthma deaths at ages 5 to 34 years that were certified by coroners increased from 35% in 1959 to 55% in 1966. The proportion of deaths from all causes certified by coroners over this period is not available separately for different age groups, but there is no reason to suppose that the proportion has increased differentially in this age group, and for all ages it has remained approximately 10%. It appears probable, therefore, that the mode of death from asthma at young ages has changed. In the absence of evidence to the contrary, it would seem that an increase in the case fatality rate is the most likely explanation of the increased mortality rate, and we have accepted this as a working hypothesis.

#### **Environmental Hazards**

Several factors could be responsible. Changes in the prevalence of environmental hazards could cause patients with asthma to be more severely affected and so could result in an increased mortality. Alternatively, new methods of management of asthmatic patients might produce temporary symptomatic relief, but increase the hazards of dying from the disease later.

Morbidity studies in New Orleans, U.S.A., have suggested that asthma can reach epidemic levels under particular conditions of atmospheric pollution (Weill et al., 1965), but it is difficult to believe that this could be a factor in England. Certainly the increase could not be due to smoke pollution, which has decreased in English towns over the last decade, nor could it be attributed to pollution with sulphur gases, which has remained approximately constant (Ministry of Technology, 1967). Motor traffic has increased considerably, and one of the constituents of motor fumes could perhaps have had a harmful effect. If this were the case, however, a substantial difference in mortality would be expected between urban and rural areas, and we have failed to find any evidence of this in the national mortality data for 1966. The death rate was 2.0

per 100,000 persons aged 5 to 34 years in conurbations, 3.0 in urban areas of more than 100,000 population, 2.2 in urban areas of under 50,000 population, and 1.9 in rural districts.

Other environmental hazards are associated with smoking and occupation, but these cannot be responsible for changes that have been observed characteristically at ages 10 to 14 years in both sexes.

#### New Methods of Treatment

Substantial advances in the management of respiratory failure from a variety of chronic pulmonary diseases have been made in the last 15 years (Detty, 1966), and new methods of both emergency and long-term therapy have been introduced for the treatment of asthma. Corticosteroids were introduced into the management of the disease in 1952, but the increase in mortality did not begin until nine years later. This discrepancy, however, is not sufficient to exculpate them entirely. The frequent and prolonged use of corticosteroids spread slowly, and the risk of harmful effects may be at a maximum only after patients have been under treatment for several years. A much closer correlation obtains with the use of pressurized aerosols containing sympathomimetics. These were introduced in England and Wales in 1960 and began to gain wide acceptance in 1961; and in the next five years their consumption is estimated to have increased more than fourfold (Ministry of Health, unpublished data). The closeness of the correlation justifies inquiry into the possible harmful effect of the preparations, but a temporal correlation of this sort, taken by itself, is a poor basis for drawing conclusions about cause and effect.

If either of these forms of therapy is to be considered as a possible cause of an increased fatality rate, it will be necessary to inquire why a similar effect has not been recorded in other countries where they have also been widely used. It may be, however, that a large increase in mortality has not been recorded in some of those countries where the mortality from asthma was initially much lower than in Britain, because similar deaths have been, and currently still are, attributed to other causes. In New Zealand the size of the population is so small that chance factors might obscure the evidence of even a substantial increase in risk. It is notable, however, that since 1959 an increase in the mortality has been recorded at ages 10 to 19 years widely throughout the world. At these ages children have begun to act independently and may be particularly prone to misuse a self-administered form of treatment.

#### Summary

The mortality attributed to asthma has increased annually in England and Wales from 1960 to 1965. The increase is more pronounced at ages 5 to 34 years than at older ages and is most pronounced at ages 10 to 14 years. In this last age group the mortality increased nearly eight times in seven years, and in 1966 asthma accounted for 7% of all deaths.

No comparable increase has been observed in any other country, but smaller increases at ages 10 to 19 years have been observed in Australasia, Japan, western Europe, and the United States.

There is no evidence to suggest that there has been any change in diagnostic habits, certification of deaths, or methods of classification which could account for the increase in Great Britain, and it is concluded that the increase is real.

General practitioners' records provide no evidence of an increase in prevalence and it seems probable that there has been an increase in case fatality.

No environmental hazards are known which could have increased the severity of the disease, and the possibility has to be considered that the increase may be due to new methods of

British Medical Journal

treatment. Corticosteroids have been used increasingly since 1952, and in Great Britain the use of pressurized aerosols containing sympathomimetics has increased rapidly since 1960.

Addendum.—Since this paper was submitted figures for 1966 in New Zealand supplied by the Public Health Statistician for New Zealand have been made available to us by Dr. These reveal an apparent increase in deaths attributed to asthma for the age group 9-54 years. Agespecific death rates are not yet available, but Dr. Gandevia suggests that an upward trend in mortality may now be occurring (Gandevia, personal communication).

We are grateful to the Registrar General of England and Wales for supplying many of the data, and for supplying them with minimal delay. We are grateful also to the Ministry of Health for information about the sale of aerosol bronchodilators; and to Miss A. M. Hetzel, Chief of the Statistical Resources Section of the Division of Vital Statistics, U.S. Public Health Service, Dr. B. Gandevia, Associate Professor in Thoracic Medicine, the Prince Henry Hospital, Little Bay, New South Wales, Professor S. Koller, Professor of Medical Statistics, University of Mainz, and Dr. D. L. Crombie,

Director of the Records and Statistics Unit of the Royal College of General Practitioners, for information about the mortality from asthma in the United States, Australia, and the German Federal Republic, and for morbidity data in Britain.

Dr. F. E. Speizer was supported by the National Center for Air Pollution, Bureau of Disease Prevention and Environmental Control, U.S. Public Health Service.

#### REFERENCES

Detty, T. L. (1966). Management of Chronic Obstructive Lung Diseases, Public Health Service Publication, No. 1457, Washington.
Ford, R. M. (1966). Med. J. Aust., 2, 196.
Fry, J. (1962). Morbidity Statistics from General Practice, Vol. 3, pp. 15-33. H.M.S.O., London.
Gandevia, B. (1967). Brit. med. J., 2, 441.
Greenberg, M. J., and Pines, A. (1967). Ibid., 1, 563.
Kessler, A., and Geller-Bernstein, C (1966). J. Amer. med. Ass., 196, 458.

458.
Ministry of Technology (1967). The Investigation of Atmospheric Pollution 1958-1966: 32nd Report. H.M.S.O., London.
Richards, W., and Patrick, J. R. (1965). Amer. J. Dis. Child., 110, 4.
Smith, J. M. (1966). Lancet, 1, 1042.
Weill, H., Ziskirdj, M. M., Derbes, V. J., Horton, R. J. M., McCaldin, R. O., and Dickerson, R. C. (1965). Arch. environm. Hlth, 10, 148.
World Health Organization (1966). Epidem. vital Statist. Rep., 19, 525.

# Investigation into Use of Drugs Preceding Death from Asthma

F. E. SPEIZER,\* M.D.; R. DOLL, M.D., F.R.C.P., F.R.S.; P. HEAF, M.D., F.R.C.P.; L. B. STRANG, M.D., F.R.C.P.

Brit. med. J., 1968, 1, 339-343

The annual number of deaths attributed to asthma has increased progressively in England and Wales since 1960. The increase has been substantial at all ages, but has been most pronounced in adolescence and young adult life. Between 1959 and 1966 the death rate increased three times at ages 5 to 34 years and nearly eight times at ages 10 to 14 years. Possible reasons for this change have been examined previously, when it was concluded that the increase was real and likely to be due, in large part, to changes in treatment leading to an increased case fatality (Speizer, Doll and Heaf, 1968). We have therefore sought information about the mode of death and the method of treatment used during and preceding the terminal illness in a consecutive series of deaths attributed to asthma in young persons.

## Data

Copies of death certificates were provided by the Registrar General for all deaths in persons aged 5 to 34 years which were registered in England and Wales in the period 1 October 1966 to 31 March 1967, and in which asthma was described as the underlying cause. On receipt of the certificates, which was usually within two months of the date of death, we sought from the local executive councils, the coroners who had signed the certificates, or the hospitals where the deaths were recorded, the names of the general practitioners on whose lists the patients were registered. A standard questionary was then mailed to the general practitioner inquiring about the therapy the patient had received during and before the terminal illness, and whether death had been anticipated. When death was recorded at

Requests for reprints should be addressed to Dr. R. Doll, University College Hospital Medical School, 115 Gower Street, London W.C.1.

hospital a similar questionary was also mailed to the hospital physician. At the time the inquiry was begun interest centred on the possible effect of corticosteroids and no direct questions were included about the use of pressurized aerosols. When death had been certified by a coroner, or the death certificate indicated that a post-mortem examination had been carried out, inquiries were also made about the necropsy findings.

The number of death certificates received and the number of questionaries returned are shown in Table I. In four instances no inquiries could be made as the name of the relevant general practitioner could not be ascertained. Two physicians did not respond to multiple inquiries, and one knew nothing about the patient, who had only just been entered on his list, and returned a blank questionary. In all, therefore, we obtained information relating to 96% of the deaths (177 out of 184). The forms were, in general, completed fully and carefully and many practitioners provided a great amount of detailed information. All the information requested was not, however, always available and some data refer to slightly smaller total numbers.

Fifty-two deaths were recorded in hospital and letters were sent to 52 hospital consultants. All replied. Few could provide any information beyond that associated with the management of the terminal episode, and six of the question-

TABLE I .- Response to Inquiries

	No. of	Questionaries to:					
Death		General	Practitioner	Hospital Consultant			
Certified by	Deaths N		No. Returned	No. Sent	No. Returned		
General practitioner Coroner Hospital consultant	44 109 31	43 106 31	43 104 31	21 31	21 31		
All sources	184	180*	178†	52	52‡		

<sup>\*</sup> U.S. Public Health Service Fellow, Medical Research Council's Statistical Research Unit.

<sup>†</sup> Director, Medical Research Council's Statistical Research Unit. † Chest Physician, University College Hospital, London W.C.1. § Professor of Paediatrics, University College Hospital Medical School, London W.C.1.

<sup>\*</sup> Four physicians not located. † Including one questionary returned blank. ‡ Including six questionaries returned blank.