Diurnal Variation in Ventilatory Capacity

An Epidemiological Study of Cotton and other Factory Workers employed on Shift Work

JOAN WALFORD, B. LAMMERS, R. S. F. SCHILLING, D. VAN DEN HOVEN VAN GENDEREN, and Y. G. VAN DER VEEN

From the London School of Hygiene and Tropical Medicine and the Almelo Industrial Medical Service, The Netherlands

The change in F.E.V._{0.75} during a working shift was studied in a random sample of 473 men employed in three cotton mills in The Netherlands working a three-shift system. Results were also obtained for 198 men, not exposed to industrial dust, who were working in a biscuit factory and two textile factories in the same area. The men were seen only during the shift on which they were working at the time of the study.

Men with byssinosis gave a typical picture of the effects of cotton dust on susceptible workers: a generally low F.E.V. with a marked reduction during the shift; -0.16 l. on the early morning shift, and -0.25 l. and -0.33 l. respectively on the afternoon and night shifts.

Men without byssinosis in the card and blow rooms showed mean changes in F.E.V. during the shifts similar to those of men working in the spinning room: a slight rise in the early morning shift of +0.02 l. followed by a fall in both afternoon and night shifts in the region of -0.10 litres. This pattern of change was also found among the workers in the non-dusty factories. The rise in the early shift cannot be explained by the clearing of mucus from the air passages; cotton workers without respiratory symptoms and men in the non-dusty factories who did not produce sputum still showed an increase in F.E.V. during the early shift, though less marked than that of men with respiratory symptoms or who produced phlegm.

The evidence suggests that a diurnal variation in lung function exists and should be taken into consideration both in epidemiological studies and when ventilatory capacity tests are used in periodic medical examinations.

Tests of ventilatory capacity are being used increasingly to measure short- and long-term effects on respiratory function of exposure to air pollutants (McKerrow, McDermott, Gilson, and Schilling, 1958; Batawi, Schilling, Valić, and Walford, 1964; Waller and Lawther, 1957). They have also been used to assess the efficacy of antibiotics and antispasmodics in the treatment of chronic bronchitis (Fletcher, Elmes, Fairbairn, and Wood, 1959; Wood and Meadows, 1963). If valid conclusions are to be drawn from the use of these tests, it is important to know the extent to which the ventilatory capacity varies during the day in both normal subjects and those with respiratory disease.

It has been found that patients with chronic bronchitis have a diurnal variation in ventilatory capacity, the test values being lowest in the early morning and usually rising to their highest level by mid-day (Lewinsohn, Capel, and Smart, 1960; Gregg, 1964). Lewinsohn and his colleagues found a similar but less marked diurnal rhythm in the forced expiratory volume (F.E.V.) of five healthymen. These and other studies of diurnal change in lung function have been based on the observations of relatively small numbers of patients over a limited period of the 24-hour cycle (Cinkotai and Thomson, 1966; McDermott, personal communication).

As part of a recent epidemiological study of 1,014 male cotton workers in The Netherlands, a random sample of 473 men was selected, and the forced expiratory volume over 0.75 sec. (F.E.V. $_{0.75}$) was measured at the beginning and end of three separate shifts covering the 24-hour cycle. This provided data enabling changes in ventilatory capacity on each shift to be studied for two main occupational groups—card and blow room workers

Received for publication October 14, 1965.

and spinners. The workers changed shifts at weekly intervals, and ideally observations should have been made on groups of men followed through all three shifts. Since the survey was not designed specifically to measure diurnal changes the men were only seen during the shift on which they were working at the time. This restricted the conclusions that could be drawn from the data, but there was no reason to suppose that observations made on separate groups would introduce bias into the results or materially affect the general pattern of diurnal variation.

Heavy exposure to cotton dust in card rooms is known to cause a fall in ventilatory capacity during the work shift, which is particularly marked in those with byssinosis (McKerrow *et al.*, 1958; Batawi *et al.*, 1964). In this study 55% of the cotton workers were employed in card and blow rooms. The remainder worked in spinning rooms in which the concentrations of respirable dust were low compared with the card rooms. To avoid the possibility of even slight exposure to cotton dust obscuring a natural diurnal change the investigation was extended to three other factories with no dust hazard.

Factories and Populations

The factories in which these studies were made are situated in The Netherlands near the German border. The three cotton mills spin medium quality cotton with comparatively low concentrations of dust in the card and blow rooms, namely, 2.7 mg./m.^3 total dust and 0.2 mg./m.^3 fine dust (particles less than 7 μ). In the survey of the total mill population the prevalence of byssinosis was found to be 17% in the card and blow rooms and less than 2% in the spinning rooms (Lammers, Schilling, and Walford, 1964). This is much lower than that found in Lancashire cotton mills spinning coarse grades of cotton.

In addition to the 473 cotton workers, a sample of 336 male workers not exposed to cotton dust was selected randomly from a biscuit factory and two textile factories, one engaged in weaving and the other in dyeing and finishing. Owing to technical faults in the use of the spirometer by one observer, 91 men had to be excluded from the analysis. Since the allocation of workers to observers was random there is no reason to believe that their exclusion introduced any systematic error into the results. With 35 absentees, three refusals, and nine unreliable or incomplete lung function tests, the final analysis is based on 198 men.

All six factories work a three-shift system; the early shift lasts from 6.00 a.m. to 2.00 p.m., the late

shift from 2.00 p.m. to 10.00 p.m., and the night shift from 10.00 p.m. to 6.00 a.m. Usual sleeping hours do not change very much while men are working on the early and late shifts; it is only on the night shift that the workers have to sleep during the day and their physiological cycle is likely to be disturbed.

Methods

Respiratory Function Tests The F.E.V. 0.75 was measured with a spirometer and timer at the beginning and end of each shift, the length of time between the two tests averaging seven hours. On a previous occasion each subject had been instructed in the correct method of blowing. For each set of tests the mean of three measurements was used after two practice blows. At the beginning and end of each shift the spirometer was calibrated. The temperature of the water in the spirometer was taken before each set of tests to enable a correction of gas volume to be made if necessary. Comparison of the two temperature readings showed that for some individuals the first temperature reading was 1 °C. lower than the second and for others 1 °C. higher; for a few it was 2°C, higher. Since at maximum the correction would have been in the order of 0.9% none was made.

Respiratory Symptoms The respiratory symptoms of the cotton workers were recorded by using the Medical Research Council's questionnaire on chronic bronchitis; it was extended to include questions concerning complaints of chest tightness on Mondays, the characteristic symptom of byssinosis.

Respiratory symptoms were not recorded for workers in the non-dusty factories, but a sputum survey was undertaken in a sample of 122 workers. Each worker was given an empty bottle and asked to collect the sputum produced in the first hour after getting up. Thus it was possible to compare ventilatory capacity change during the shift for those with and those without sputum.

Results

Change in F.E.V. during Shifts in Workers with and without Byssinosis

Cotton Workers Out of 256 card and blow room workers, 57 had symptoms of byssinosis. Since exposure to cotton dust is known to affect the ventilatory capacity of byssinotics to a much greater extent than that of normal workers, these men were separated from the other card and blow room workers. Of the 217 men in the spinning room only five had symptoms of byssinosis and were excluded from the analysis. This left three main groups crossclassified by shift. There were some differences in the mean age of the groups, and since the F.E.V. is

TABLE I

MEAN INITIAL F.E.V.₀₋₇₅, Adjusted for Age and Stem Height, and Mean Change During the Shift in Workers with Byssinosis in the Card and Blow Rooms and Without Byssinosis in the Card and Blow Rooms and Spinning Room

Shift	Card and Blow Room Workers					Card and Blow Room Workers					Spinning Room Workers				
	with Byssinosis					without Byssinosis					without Byssinosis				
	No. of Wkrs.	Mean Age (years)	Mean F.E.V. _{0.75} (litres)		Mean Change (l.)	No. of Wkrs.	Mean Age . (years	Mean F.E.V. _{0.75}) (litres)		Mean Change (l.)	No. of Wkrs.	Mean Age (years)	Mean F.E.V. _{0.75} (litres)		Mean Change (l.)
			Unad- justed	Ad- justed	-			Unad- justed	Ad- justed	-			Unad- justed	Ad- justed	-
Early	23	42	2·67	2·83	-0.16	69	39	2·94	3·02	+0.02	68	38	3·07	3·13	+0.02
Late	22	41	2·73	2·85	-0.25	68	39	3·13	3·21	-0.13	80	38	2·98	3·07	-0.10
Night	12	41	2·66	2·87	-0.33	62	35	3·14	3·09	-0.10	64	37	3·16	3·19	-0.10

related negatively to age and positively to height, the mean of the initial F.E.V. in each group was adjusted so that the ventilatory capacities measured before exposure to cotton dust would be comparable. The adjustments were made by calculating the regression of the initial F.E.V. on age and stem height, and correcting the observed mean F.E.V. to give the expected value for a standard age of 38 vears and a stem height of 89 cm. A common regression for cotton workers and workers in nondusty factories was not used as the separate regressions for the two groups showed a statistically significant difference (P < 0.01). The regression relationship for cotton workers was given by the equation $\bar{Y} = -1.271 - 0.036X_1 + 0.064X_2$ where X_1 = age in years, and X_2 = stem height in cm. No corresponding adjustment was made to the mean change during the shift since this was found to have no statistical relation to age or to the initial F.E.V.

Adjusted mean initial F.E.V.s and the mean changes during the shift are shown in Table I. The long-term effect of exposure to cotton dust on ventilatory capacity is reflected in the low initial F.E.V.s of the card and blow room workers with byssinosis. They also have a marked reduction in F.E.V. during all three shifts, typical of the acute effects of cotton dust exposure on susceptible workers. The reduction is, however, least on the early morning shift and greatest on the night shift and cannot be explained by differences in levels of dust exposure on the three shifts. The mean concentrations of fine dust were similar on each shift, and the mean concentration of total dust was highest on the early shift. Within each shift the differences in mean change in F.E.V. between byssinotics and the other two groups of cotton workers are statistically significant at levels of confidence ranging from 0.05 to 0.001.

In the two groups without byssinosis, the pattern

of change over the three shifts is almost identical, the early shift showing a rise in F.E.V. and the other two shifts a fall. Within each group the differences between the early and late shifts, and between the early and night shifts, are statistically significant (P < 0.0I).

Other Factory Workers The results from each of the three non-dusty factories were first examined separately but were similar enough to allow them to be grouped together. The mean F.E.V.s were adjusted for age and stem height using the regression equation $Y = 0.937 - 0.026X_1 + 0.037X_2$ calculated from the pooled data of the three factories.

The changes in F.E.V. during the shift for the factory workers are similar to those found in the cotton workers except that the rise in F.E.V. during the early morning shift is greater (Table II). The

TABLE II

MEAN INITIAL F.E.V. $_{0.75}$, adjusted for Age and Stem Height, and Mean Change during the Shift in Workers in Three Non-Dusty Factories

Shift	No. of	Mean Age	Mean F (litres)	<i>E.V.</i> 0.75	Mean Change	
	w or rers	(years)	Unadju	sted Adjusted	(1.)	
Early	79	38	3.27	3.26	+0.09	
Late	72	38	3.31	3.32	-0.14	
Night	47	38	3.13	3.12	-0.09	

differences between the early and late shifts, and between the early and night shifts, are statistically significant (P < 0.001).

The similarity in the pattern of diurnal change for workers in the non-dusty factories and for cotton workers without byssinosis can be seen more clearly in the Figure.



FIGURE. Mean change in F.E.V._{0.75} during shifts for cotton workers with and without byssinosis and workers in non-dusty factories.

Effect of Other Respiratory Symptoms on F.E.V. Change

Cotton Workers Since it is known that bronchitics show a rise in ventilatory capacity after the clearance of early morning phlegm, it seemed likely that the rise in F.E.V. during the early morning shift, found in workers without byssinosis, was caused by the inclusion of men with other respiratory symptoms. As the card and blow room workers without byssinosis showed a pattern of change in F.E.V. similar to those in the spinning room, the two groups were combined to examine the effects of cough and phlegm on F.E.V. change. For the combined group the rise in F.E.V. during the early morning shift is more marked among those with respiratory symptoms, the fall during the late shift less marked, and during the night shift the fall is much the same whether respiratory symptoms are present or not (Table III). These results suggest that although the ventilatory capacity of those on the early and late shifts with persistent cough or phlegm does get relatively better as a result of clearing the air passages as the day goes on, the underlying diurnal rhythm is similar to that of workers without respiratory symptoms.

Among the byssinotics there is no appreciable difference between the F.E.V. changes during the shift for those with and without symptoms of persistent cough and/or phlegm (Table IV).

TABLE III

Mean Initial F.E.V._{0.75}, adjusted for Age and Stem Height, and Mean Change during the Shift for Non-Byssinotic Card and Blow and Spinning Room Workers with and without Persistent Cough and/or Phlegm

Shift Gard, Blow, and Spinning Koom Workers without Bys	ssinosis
---	----------

	With Cou	gh and/or I	Phlegm			Without C	Cough and/d	or Phlegm		
	No. of Workers	Mean Age (years)	Mean F (litres)	E.V.0.75	Mean Change (l.)	No. of Workers	Mean Age (years)	Mean F (litres) Unadius	.E.V.0.75	Mean Change (l.)
 Early	29	43	2.66	2.91	+0.06	108	37	3.10	3.15	+0.01
Late Night	35 14	39 38	2·69 2·68	2·81 2·84	-0.05 -0.08	113 112	38 36	3·16 3·21	3·23 3·18	-0·13 -0·10

TABLE IV

MEAN INITIAL F.E.V.0.75, ADJUSTED FOR AGE AND STEM HEIGHT, AND MEAN CHANGES DURING THE SHIFT FOR BYSSINOTIC CARD AND BLOW ROOM WORKERS WITH AND WITHOUT PERSISTENT COUGH AND/OR PHLEGM Card and Blow Room Workers with Byssinosis

	With Cough and/or Phlegm						Without Cough and/or Phlegm						
	No. of	Mean Age	Mean F (litres)	.E.V. _{0.75}	Mean Change	No. of	Mean Age	Mean F (litres)	.E.V. _{0.75}	Mean Change			
	Workers	(years)	Unadjus	ted Adjusted	(1.)	Workers	(years)	Unadjus	sted Adjusted	- (<i>l</i> .) !			
Early	9	45	2.73	3.02	-0.12	14	40	2.63	2.70	-0.14			
Late	II	47	2.20	2.57	-0.54	11	35	3.20	3.15	-0.26			
Night	6	42	2.38	2.71	– o·28	6	40	2.94	3.04	-0·37			

Other Factory Workers Of the 122 workers in non-dusty factories who participated in the sputum survey, the 26 men who produced sputum had a much lower F.E.V. than those who did not (Table V). They had a greater rise in F.E.V. in the early shift and a greater fall in the other two shifts than those who did not produce sputum (Table VI).

Shift

Since cigarette smoking may be a factor in the production of persistent cough and phlegm and may have both an acute and chronic effect on F.E.V., ventilatory capacity changes among the cotton workers were examined in relation to smoking habit. The numbers in the sub-groups were very small, but there was no consistent trend in relation to either the type of smoking or the amount smoked.

Variation in Ventilatory Capacity by Day of Week and Season In several recent investigations, the acute effects of exposure to cotton or flax dust on ventilatory capacity have been measured on the different days of the week for the same subjects. They show that on the average a greater reduction in ventilatory capacity during the shift occurs on a Monday (the first day back at work after the weekend break) than on other work days (McKerrow *et al.*, 1958; Bouhuys, van Duyn and van Lennep, 1961; Bouhuys, Hartogensis, and Korfage, 1963; Carey, Elwood, McAulay, Merrett, and Pemberton, 1963; Batawi *et al.*, 1964).

If the changes in ventilatory capacity are influenced by the day of the week on which the tests are made, the findings which we have described could have been biased by the choice of day for the tests. However, it could be assumed that the allocation of the subjects to the day of the test was random, and examination of the data showed no

TABLE V

MEAN INITIAL F.E.V._{0.75}, ADJUSTED FOR AGE AND STEM HEIGHT, FOR WORKERS IN NON-DUSTY FACTORIES INCLUDED IN SPUTUM SURVEY

Shift	With Sp	utum			Without	Sputum			Total			
No. Mean of Age		Mean Age	n Mean F.E.V. _{0.75} (litres)		No. of	Mean Age	Mean Mean F.E.V. _{0.75} Age (litres)		No. Mean of Age		Mean F.E.V. _{0.75} (litres)	
	w orkers	(years)	Unad- justed	Ad- justed	w or rets	(years)	Unad- justed	Ad- justed	w or rers	(years)	Unad- justed	Ad- justed
Early	15	40	3.02	3.08	35	39	3.34	3.32	50	39	3.24	3.27
Late	7	40	2.92	2.92	43	37	3.42	3.42	50	37	3.35 -	3.35
Night	4	35	3.22	3.17	18	38	3.30	3.30	22	38	3.29	3.28

TABLE VI

MEAN CHANGE IN F.E.V.₀₋₇₅ DURING SHIFT FOR WORKERS IN NON-DUSTY FACTORIES INCLUDED IN SPUTUM SURVEY

Shift With Sputum		1	Without Sput	tum	Total	ıl		
	No. of Workers	Mean Change (litres)	No. of Workers	Mean Change (litres)	No. of Workers	Mean Change (litres)		
Early	14	+0.15	35	+0.02	49	+0.08		
Late	6	-0.55	43	-0.14	49	-0.12		
Night	4	-0.19	16	-0.02	20	0.08		

Three men did not have the F.E.V. measured at the end of the shift and one had unreliable readings.

TABLE

association between the change in F.E.V. and the day of the test. Thus our results cannot be explained by any bias in the choice of day.

McKerrow (1964) measured over a period of three years the indirect maximum breathing capacity (I.M.B.C.) of 28 ex-miners with pneumoconiosis working in a light engineering factory. He showed a seasonal variation in ventilatory capacity that could be described by a sine curve with a period of 12 months; the lowest readings were recorded in February and the highest in August.

In our enquiry the cotton workers were tested in February, April, May, and October; the workers in the non-dusty factories were all tested in September. When the data for the cotton workers were examined by month as well as shift, the mean initial F.E.V. adjusted for age and stem height showed no consistent seasonal variation. The mean change in F.E.V. during the shift showed only one statistically significant difference between the months; this was in the workers without byssinosis on the early shift in February, who had a mean decrease in F.E.V. (Table VII). There is no simple explanation for this surprising result. However, it does not materially affect the general pattern and there is no evidence that seasonal variations had any appreciable influence on our results.

Discussion

The increase in the ventilatory capacities of the Dutch shift workers between 6.00 a.m. and 2.00 p.m. is similar to the findings of Lewinsohn *et al.* (1960) in their more intensive studies of small groups of patients and normal subjects. There is fortuitous evidence of diurnal variation in ventilatory capacity from other field surveys. Bouhuys *et al.* (1963),

studying mean changes in forced expiratory volume (F.E.V.0.75) during the shift in flax workers, found a small increase during the early shift and a decrease during the afternoon shift. They remarked on the difficulty of explaining these divergent results. In the first published study of the acute effects of cotton dust exposure on ventilatory capacity, McKerrow and his colleagues (1958) used for comparison a group of coalminers exposed to an average total dust concentration greater than that in the cotton mill, but employed on the early shift, 7.00 a.m. to 2.00 p.m. In contrast to the cotton workers, who were examined between 7.30 a.m. and 4.30 p.m., the I.M.B.C. of the miners increased and their airways resistance decreased during the shift. It was concluded that the respiratory impairment shown by the cotton workers was caused by the mill dust. McDermott (personal communication), measuring airways resistance with the body plethysmograph in nine normal subjects, found on the average that it fell between 10.00 a.m. and 3.00 p.m. and then rose between 3.00 p.m. and 11.00 p.m. Zuidema (1965) has recorded similar results, measuring diurnal variation in airway resistance in 10 patients with asthma. He used the interrupter technique, peak flow, vital capacity, and forced expiratory volume (F.E.V.1.0) and took readings at four-hourly intervals from 4.00 a.m. to 8.00 p.m. Airway resistance generally decreased between 4.00 a.m. and mid-day, increased between mid-day and 8.00 p.m., and also between 8.00 p.m. and 4.00 a.m.

It is known that sufferers from chronic bronchitis show a rise in ventilatory capacity during the morning. In our enquiry workers on the early shift with respiratory symptoms show a greater increase in ventilatory capacity during the shift than those without symptoms. However, clearing the mucus

TABLE VII

MEAN CHANGE IN F.E.V.0.75 DURING THE SHI	FT BY TIME OF YEAR FOR COTTON WORKERS
IN CARD, BLOW, AND	SPINNING ROOMS

Cotton Workers Month of Tests

	February		April + Ma	iy	October		
	No. of Workers	Mean Change in F.E.V. _{0.75} (l.)	No. of Workers	Mean Change in F.E.V. _{0.75} (l.)	No. of Workers	Mean Change in F.E.V. _{0.75} (l.)	
Without byssinos	is						
Early shift*	34	-0.02	55	+0.06	48	+0·04	
Late shift	28	-0.11	55	-0.10	65	-0.11	
Night shift	29	-0.10	57	-0.13	40	-0.04	
With byssinosis				-	-	-	
Early shift	4	-0.11	16	-0.13	3	-0.32	
Late shift	8	-0.50	13	-0.22	4	-0.34	
Night shift	3	-0.00	ž	-0.43	8	-0.32	

*Statistically significant difference in diurnal change between February and April + May. t = $2 \cdot I2$ P < 0.05

148 Joan Walford, B. Lammers, R. S. F. Schilling, D. van den Hoven van Genderen, and Y. G. van der Veen

from the airways cannot be entirely responsible for the rise during the shift since the same upward trend is shown by those who are symptom-free. The decrease in F.E.V. which follows later in the day could be due to air pollutants in the working environment, but the similarity in the pattern of change shown by cotton card room workers without byssinosis and by spinners, as well as by workers in the non-dusty factories, does not support this suggestion.

Diurnal rhythm is known to occur in several physiological functions such as body temperature (Kleitman and Ramsaroop, 1948), blood pressure (Mueller and Brown, 1930; Richardson, Honour, Fenton, Stott, and Pickering, 1964), haemoglobin levels (Elwood, 1962), and diffusing capacity of the lung (Cinkotai and Thomson, 1966). Menzel (1962) gives an extensive account of physiological function showing diurnal changes, including the vital capacity and the forced expiratory volume which show a decrease during the night. Burger, van Alphen de Veer, Groot Wesseldijk, van den Graaf, and Doornbosch (1958), in an investigation on shift workers, found the respiratory minute volume during exertion to be significantly lower in workers on the night shift compared with day workers. This was due to a lower frequency of respiration as well as a smaller tidal volume.

Pulmonary ventilation is known to increase when body temperature is raised by exposure to a hot environment, but it seems unlikely that the changes in ventilatory capacity found in this study could be entirely due to the normal diurnal variation in body temperature. Little seems to be known of the effects on ventilatory capacity of fatigue or changes in metabolic activity, but the rise in airways resistance found in the latter part of the day by McDermott is unlikely to be due to fatigue since this test does not require physical effort.

The results we have presented are based on F.E.V. readings taken at the beginning and end of the shift and on the performance of different groups of workers on each shift. It is not possible to assess the effects of the weekly change of shift, which may be considerable for night workers who are likely to take a few days to adjust to a new physiological rhythm (Bonjer, 1961). Nevertheless, the consistent pattern we have found in ventilatory capacity suggests that a diurnal rhythm in lung function exists. To discover its form more precisely, and the influence of environmental and personal factors upon it, would require a larger and more detailed study of shift workers designed for the purpose. It may then be possible to estimate the effects on ventilatory capacity of the extraneous factors and to eliminate them, either by direct control or by statistical

methods, thus enabling valid comparisons to be made between groups tested at different times of the day.

Until more is known of the diurnal rhythm in lung function it seems safer, when comparing groups in epidemiological studies, to take measurements at approximately the same time of day. Similar care is needed when using ventilatory capacity tests in periodic medical examinations.

We are specially indebted to the management and workers of the factories in which this study was made.

We also thank Messrs. G. Koop, A. J. van Leiden, and H. Wieldraayer for assisting with this survey, and Miss Sheila Farrow for helping to analyse the data.

We have had helpful criticisms in preparing this paper from colleagues in the London School of Hygiene and Tropical Medicine, especially Dr. M. Thomson, and from Dr. C. B. McKerrow and Dr. A. Bouhuys.

We are grateful for a grant to one of us (R.S.F.S.) from the Medical Research Council to undertake this research.

REFERENCES

- Batawi, M. A. El, Schilling, R. S. F., Valić, F., and Walford, J. (1964). Brit. J. industr. Med., 21, 13.
- Bonjer, F. H. (1961). Proc. 13th int. Congr. Occup. Hlth, New York, 1960, p. 848.
- Bouhuys, A., van Duyn, J., and van Lennep, H. J. (1961). Arch. environm. Hlth, 3, 499.
- Hartogensis, F., and Korfage, H. J. H. (1963). Brit. J. industr. Med., 20, 320.
- Burger, G. C. E., van Alphen de Veer, M. R., Groot Wesseldijk, A. Th., van den Graaf, M. H. K., and Doornbosch, A. (1958). Proc. 12th int. Congr. Occup. Hlth, Helsinki, 1957, Vol. 3, p. 126.
- Carey, G. C. R., Elwood, P. C., McAulay, I. R., Merrett, J. D., and Pemberton, J. (1963). A report on byssinosis in flax workers in Northern Ireland to the Ministry of Labour and National Insurance of the Government of Northern Ireland.
- Cinkotai, F. F., and Thomson, M. L. (1966). In the press.
- Elwood, P. C. (1962). Clin. Sci., 23, 379.
- Fletcher, C. M., Elmes, P. C., Fairbairn, A. S., and Wood, C. H. (1959). Brit. med. J., 2, 257. Gregg, I. (1964). J. Coll. gen. Practit., 7, 199.
- Kleitman, N., and Ramsaroop, A. (1948). Endocrinology, 43, I.
- Lammers, B., Schilling, R. S. F., and Walford, J. (1964). Brit. J. industr. Med., 21, 124.
- Lewinsohn, H. C., Capel, L. H., and Smart, J. (1960). Brit. med. J., 1, 462.
- McKerrow, C. B. (1964). Arch. environm. Hlth, 8, 174.
- , McDermott, M., Gilson, J. C., and Schilling, R. S. F. (1958). Brit. J. industr. Med., 15, 75.

- Mueller, S. C., and Brown, G. E. (1930). Ann. intern. Med., 3, 1190.
- Richardson, D. W., Honour, A. J., Fenton, G. W., Stott, F. H., and Pickering, G. W. (1964). Clin. Sci., 26, 445.
- Waller, R. E., and Lawther, P. J. (1957). Brit. med. J., 2, 1473. Wood, C. H., and Meadows, S. H. (1963). Ibid., 2, 1088.
- Zuidema, P. (1965). Trans. World Asthma Conference.
- Eastbourne, 1965, p. 129. Chest and Heart Association, London

Menzel, W. (1962). Menschliche Tag-Nacht-Rhythmik und Schichtarbeit. Bruno Schwabe, Basel and Stuttgart.