cancer of sites other than the lung shows a mortality of 2.04 per 1,000 in non-smokers and 2.02 per 1,000 in smokers. It reveals no gradient by amount smoked (Table XIII). In other words, the marked and steadily increasing mortality from lung cancer in association with smoking is not compensated for by a decrease in cancer of other sites. The result indicates a total mortality from cancer in the smoking groups in excess of the mortality that would have prevailed in the absence of smoking.

11. If the causes of death as certified are accepted at their face value, mortality from coronary thrombosis reveals a slight but significant relationship with smoking (Table V). Division by age, however, shows that the trend is distinct only at the youngest ages, 35–54 years (Table XV).

12. Three other causes of death show a steady increase in mortality from non-smokers to heavy smokers—chronic bronchitis, peptic ulcer, and pulmonary tuberculosis (Table XVI). Only with chronic bronchitis is the gradient statistically significant. The remaining causes of mortality reveal no trend (Table XVII).

13. From our retrospective studies of the smoking habits of nearly 1,500 patients with lung cancer and over 3,000 patients with other illnesses we concluded that if large groups of persons of different smoking habits were observed for a number of years they would reveal distinct differences in their rates of mortality from lung cancer. They would show, we believed, (1) a higher mortality in smokers than in non-smokers, (2) a higher mortality in heavy smokers than in light smokers, (3) a higher mortality in cigarette smokers than in pipe smokers, and (4) a higher mortality in those who continued to smoke than in those who gave it up. In each case the expected result has appeared in the prospective inquiry here reported. These results are evident in spite of the fact that our method of inquiry is such as constantly to *underestimate* the mortality differences. The reason for the underestimate is that our classifications are based, for the most part, upon a statement of the smoking habits at one point of time. We have seldom been able to take previous habits into account, and any subsequent changes have been unknown to us. As a result we shall sometimes have included in the light smoking group persons who had previously smoked heavily for a long time; we shall sometimes have included as "pure" pipe smokers persons who had previously smoked cigarettes and vice versa; we shall sometimes have continued to class as smokers persons who have given up. All such errors in classification must inevitably have reduced the, nevertheless, clear associations between the mortality from lung cancer and the smoking of cigarettes which we have observed in these British doctors.

This work was made possible by the co-operation of the thousands of doctors who completed our questionaries. We are most grateful to them and to the many consultants who have provided us with further details of the evidence on which the diagnosis of lung cancer was made. We are deeply indebted to the British Medical Association, who dispatched the questionaries on our behalf and who subsequently helped us in tracing the deaths of doctors; to the Registrars-General of the United Kingdom and the Registrars of the General Medical Council and of its Branch Councils in Ireland and Scotland for information about the deaths of doctors; and to the Statistical Department of the Ministry of Labour for the mechanical analysis of the results. We are grateful to Dr. R. Bignall for advice on the clinical classification of some of the deaths from lung cancer. We also offer our thanks to Mrs. Joan Bodington, Mrs. Jean Gilliland, Miss Keena Jones, and Mrs. M. Lloyd for the onerous work of sorting and analysing the mass of data.

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# AN ASSOCIATION BETWEEN SMOKING AND RESPIRATORY TUBERCULOSIS

BY


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In England and Wales mortality from respiratory tuberculosis has been falling for at least a century. The rate of decline has not been the same at all ages, however, and in the two sexes the pattern of mortality, which seventy-five years ago was not dissimilar, is now strikingly different (Fig. 1). During the decade 1871–80 mortality for both males and females was highest in early adult life. Seventy years later this is still true for females, but for males death rates in young adult life have fallen so much more rapidly than in middle and late life that maximum mortality now occurs at a much later age.

A number of partial explanations have been offered for this change in the age pattern of mortality, but they do not add up to a very convincing whole, and the sex difference remains an incompletely solved epidemiological

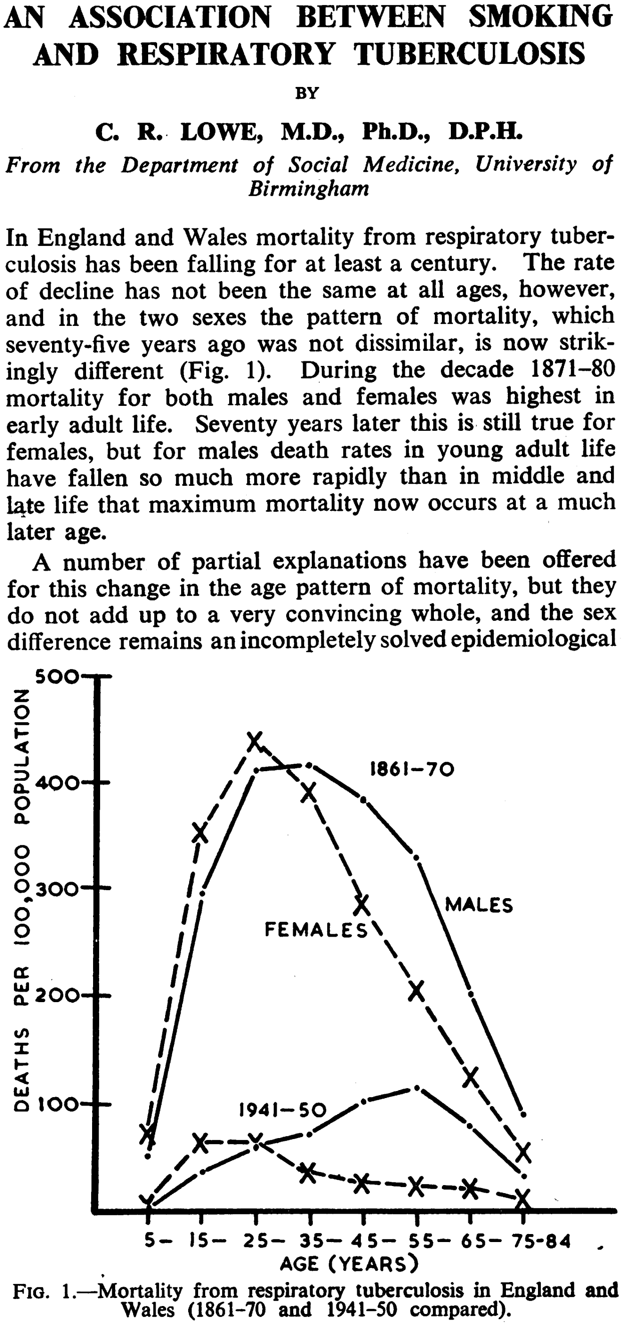


FIG. 1.—Mortality from respiratory tuberculosis in England and Wales (1861–70 and 1941–50 compared).

puzzle. The two most quoted explanations have been, first, that the difference is in part the result of a cohort or generation effect, and, second, that it is related to the degree of urbanization and the proportion of males in industrial occupations.

The cohort method of examining mortality from tuberculosis was first explored by Frost (1939) and was used again by Springett (1952), who gave a clear explanation of this rather complicated procedure. In brief, the method traces death rates experienced at successive ages by a group of persons (the "cohort") born in the same decennium (or any other convenient time interval), in contrast to the orthodox method illustrated in Fig. 1, which examines age-specific death rates of a population in a stated year (or group of years). When male death rates are examined in this way the shift of maximum mortality towards middle and late life disappears. It

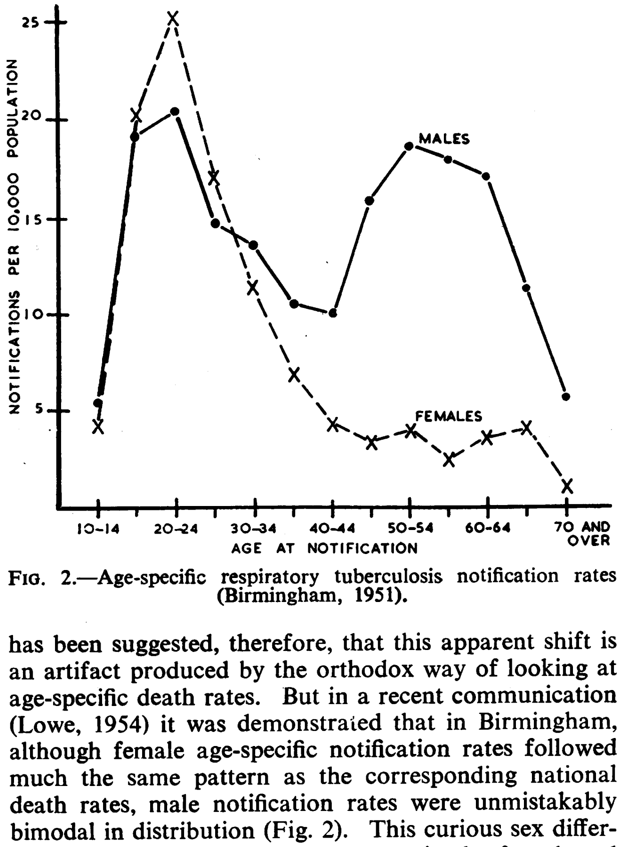


FIG. 2.—Age-specific respiratory tuberculosis notification rates (Birmingham, 1951).

has been suggested, therefore, that this apparent shift is an artifact produced by the orthodox way of looking at age-specific death rates. But in a recent communication (Lowe, 1954) it was demonstrated that in Birmingham, although female age-specific notification rates followed much the same pattern as the corresponding national death rates, male notification rates were unmistakably bimodal in distribution (Fig. 2). This curious sex difference is now becoming apparent even in the four broad age groups used for notification rates in national statistics (Registrar-General, 1955), and it is difficult to believe that this is a statistical illusion which, if the data were available, cohort analysis could explain away. In any case the cohort method of looking at death rates does not explain why in middle and late life mortality has fallen at a much slower rate in males than in females, while in early adult life, if anything, the reverse is true (Table I).

TABLE I.—*Mortality From Respiratory Tuberculosis in* 1941–50 *Expressed as a Percentage of Mortality in* 1861–70

| | Age | | | | | |
|---|---|---|---|---|---|---|
| | 15–24 | 25–34 | 35–44 | 45–54 | 55–64 | 65–74 |
| Males .. | 12·7 | 14·8 | 17·0 | 26·3 | 35·3 | 39·2 |
| Females .. | 18·7 | 15·0 | 10·0 | 9·8 | 12·4 | 17·6 |

A more plausible explanation rests upon the observation that the pattern of male mortality in late adult life appears to some extent to be related to the degree of urbanization. Dahlberg (1949) examined the recent mortality from tuberculosis in many different countries. He found that for males there was an excessive mortality in middle and late life in Germany, France, Italy, and the U.S.A., as well as in England and Wales, but that the sex difference was by no means so marked in Sweden, Norway, and Denmark. He suggested that this difference might be due to "a greater measure of urbanization in the larger countries" and in particular to the much greater risk of coming into contact with persons suffering from tuberculosis to which employment in congested and highly industrialized communities exposes the male. In addition, McDonald (1952) has demonstrated that in England and Wales the sex difference in age-mortality pattern is much more marked in London and county boroughs than in small towns and rural districts, and he believes with Dahlberg that greater opportunity for contact with infection at place of work is the probable explanation.

In recent years, however, it is becoming accepted that "a large part of the tuberculosis mortality in males in later life is due to a final breakdown of disease acquired many years earlier" (Springett, 1952). It seems unlikely, therefore, that opportunity for infection or reinfection at place of work is the principal reason for the difference between the sexes. And unless there is some inherent difference between males and females in their reaction to infection, which is, of course, possible, the explanation must lie in a sex difference in middle and late life in the risk of exposure to environmental influences that can lead to breakdown of healed or quiescent lesions. In industry men are often exposed to dust, fume, smoke, and mist hazards in a bewildering variety, and it is possible that these may in part account for a difference in rate of breakdown. But one of the most profound differences between the pulmonary environment of males and females, the degree to which the lungs are exposed to tobacco smoke, has so far been overlooked as a possible explanation. In view of the established relationship between smoking habits and cancer of the lung, in which male mortality is also relatively high, it was thought worth while to investigate the smoking habits of patients with respiratory tuberculosis.

### Method of Investigation

Since tuberculosis is a notifiable disease, it is an easy matter to identify large numbers of patients with respiratory infection. The problem of interviewing patients is also simplified by the fact that substantial numbers are to be found in sanatoria, while the majority of those living at home attend chest clinics at fairly regular intervals. In this investigation notification was accepted as the diagnostic criterion, and the sample of patients was drawn from sanatorium and chest clinic.

During February, March, and April, 1955, a social worker questioned about their smoking habits all patients occupying beds in the three principal sanatoria providing accommodation for Birmingham residents. During October, November, and December, 1955, the same social worker interviewed all patients attending the Birmingham Chest Clinic. Apart from one sanatorium patient who was too ill to be questioned and one clinic patient who refused to co-operate, there was no selection. For the purpose of this investigation it was decided to exclude non-Europeans, patients who were under 20 years of age at notification,

TABLE II.—*Source of Patients and Controls*

| Place of Interview | Males | Females | Total |
|---|---|---|---|
| Patients: | | | |
| Sanatorium .. .. .. .. | 255 | 179 | 434 |
| Chest clinic .. .. .. .. | 508 | 258 | 766 |
| Total .. .. .. .. | 763 | 437 | 1,200 |
| Controls: | | | |
| Accident hospital out-patients | 327 | 261 | 588 |
| General hospital in-patients .. | 237 | 154 | 391 |
| Total .. .. .. | 564 | 415 | 979 |

and patients who at the time of interview had not been notified. The source of the final sample of 1,200 patients is shown in Table II.

The identification of a suitable control group was more difficult. In the first place it is clear from the literature that smoking habits vary considerably with age. The advantage of an age-matched control series is, however, more than outweighed by the difficulty of collecting it, and it was decided to rely upon age-specific and age-standardized comparisons. In the second place, since a number of conditions which may lead to hospital admission are already known to be associated with smoking habits (lung cancer, chronic bronchitis, and coronary thrombosis), hospital patients, although the most accessible, are certainly not the best population from which to draw a control series. The difficulty of interviewing a large random sample of the general population is so great, however, that it was decided to use as controls certain sections of the local hospital population.

During May, 1955, the social worker interviewed all new patients attending the Birmingham Accident Hospital with minor injuries. In June and again in September of the same year she interviewed all patients occupying beds in the surgical wards of Dudley Road Hospital (a large non-teaching Birmingham hospital). Patients under 20 years of age, non-Europeans, and patients with lung cancer and respiratory tuberculosis were excluded. The source of the 979 controls is also given in Table II.

Smoking habits were recorded as the number of cigarettes per day (1 oz. (28 g.) of pipe tobacco a week was considered the equivalent of four cigarettes a day), and persons who had never smoked as much as one cigarette a day for as long as a year were entered as non-smokers (Doll and Hill, 1950). Smokers were asked how much they were smoking at present, the maximum amount they had ever smoked, the age at which they had begun to smoke, and, if they had given up smoking, the time that had elapsed since they last smoked. In addition, tuberculous patients were asked how much they were smoking immediately before notification (of which the date was recorded), and controls who were hospital in-patients were asked how much they were smoking immediately before their present illness.

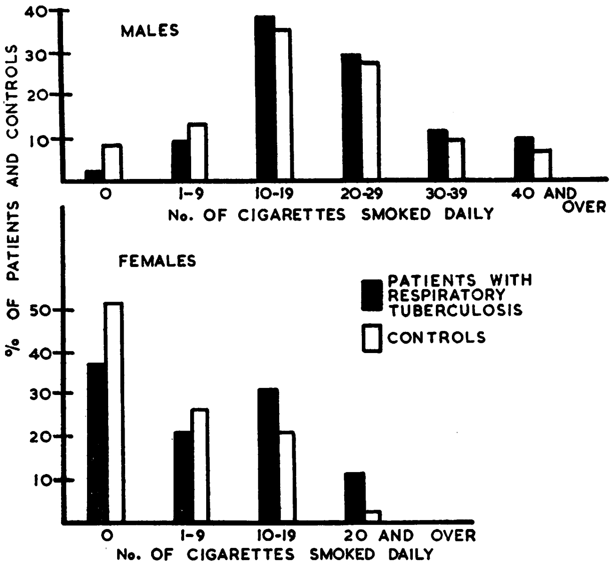


FIG. 3.—Smoking habits of patients with respiratory tuberculosis and controls compared (aged 30 years and over).

TABLE III.—*Smoking Habits of Patients and Controls Aged 30 Years and Over*

| | Males | | | | | | | Females | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | No. of Cigarettes Smoked per Day | | | | | | Total | No. of Cigarettes Smoked per Day | | | | Total |
| | 0 | 1–9 | 10–19 | 20–29 | 30–39 | 40+ | | 0 | 1–9 | 10–19 | 20+ | |
| Patients .. | 2·5 | 9·2 | 38·1 | 29·4 | 11·3 | 9·4 | 100% | 37·3 | 20·5 | 30·8 | 11·4 | 100% |
| | (13) | (48) | (198) | (153) | (59) | (49) | (520) | (69) | (38) | (57) | (21) | (185) |
| Controls .. | 8·1 | 12·9 | 35·6 | 27·4 | 9·3 | 6·7 | 100% | 51·4 | 25·7 | 20·5 | 2·4 | 100% |
| | (34) | (54) | (149) | (115) | (39) | (28) | (419) | (128) | (64) | (51) | (6) | (249) |

Males: $\chi^2_5=21\cdot2$; $P<0\cdot01$. Females: $\chi^2_3=24\cdot0$; $P<0\cdot01$.

TABLE IV.—*Smoking Habits of Sanatorium and Chest Clinic Patients Compared (Aged 30 Years and Over)*

| Source of Patients | Males | | | | | | | Females | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | No. of Cigarettes Smoked per Day | | | | | | Total | No. of Cigarettes Smoked per Day | | | | Total |
| | 0 | 1–9 | 10–19 | 20–29 | 30–39 | 40+ | | 0 | 1–9 | 10–19 | 20+ | |
| Sanatorium .. | 0·6 | 9·8 | 39·7 | 32·8 | 8·6 | 8·6 | 100% | 34·1 | 21·2 | 35·3 | 9·4 | 100% |
| | (1) | (17) | (69) | (57) | (15) | (15) | (174) | (29) | (18) | (30) | (8) | (85) |
| Chest clinic .. | 3·5 | 9·0 | 37·3 | 27·7 | 12·7 | 9·8 | 100% | 40·0 | 20·0 | 27·0 | 13·0 | 100% |
| | (12) | (31) | (129) | (96) | (44) | (34) | (346) | (40) | (20) | (27) | (13) | (100) |

Males: $\chi^2_4=3\cdot5$; $0\cdot3<P<0\cdot5$. (Male non-smokers and those smoking less than 10 cigarettes a day grouped together.)
Females: $\chi^2_3=2\cdot0$; $0\cdot7<P<0\cdot5$.

TABLE V.—*Smoking Habits of Out-patient and In-patient Controls Compared (Aged 30 Years and Over)*

| Source of Controls | Males | | | | | | | Females | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | No. of Cigarettes Smoked per Day | | | | | | Total | No. of Cigarettes Smoked per Day | | | | Total |
| | 0 | 1–9 | 10–19 | 20–29 | 30–39 | 40+ | | 0 | 1–9 | 10–19 | 20+ | |
| Accident hospital out-patients | 9·1 | 13·2 | 31·5 | 29·2 | 9·6 | 7·3 | 100% | 50·9 | 27·5 | 18·6 | 3·0 | 100% |
| | (20) | (29) | (69) | (64) | (21) | (16) | (219) | (85) | (46) | (31) | (5) | (167) |
| General hospital in-patients | 7·0 | 12·5 | 40·0 | 25·5 | 9·0 | 6·0 | 100% | 52·4 | 22·0 | 24·4 | 1·2 | 100% |
| | (14) | (25) | (80) | (51) | (18) | (12) | (200) | (43) | (18) | (20) | (1) | (82) |

Males: $\chi^2_5=3\cdot9$; $0\cdot7<P<0\cdot5$. Females: $\chi^2_2=1\cdot3$; $0\cdot7<P<0\cdot5$. (All females smoking 10 or more cigarettes a day grouped together.)

### Results

The data collected permit the smoking habits of patients and controls to be compared in a number of different ways. In the analysis which follows the number of cigarettes smoked daily by patients with tuberculosis refers to regular smoking habits immediately before notification. (In all tabular material, therefore, the age of these patients is age at notification and not age at interview.) The number of cigarettes smoked daily by controls refers, in the case of out-patients, to smoking habits at time of interview and, in the case of in-patients, to habits immediately before the present hospital illness. A small number of patients and controls had given up smoking before notification and interview (or hospital admission) respectively. These persons were classified according to the amount they were smoking immediately before they gave it up.

The essential findings of the investigation are summarized in Table III and Fig. 3. In both sexes patients of over 30 years of age with pulmonary tuberculosis showed when compared with the controls a highly significant deficiency of non-smokers and light smokers and an excess of moderate and heavy smokers (11.7% of the tuberculous males were non-smokers or had smoked less than 10 cigarettes a day, compared with 21.0% of the controls; 50.1% had smoked 20 or more cigarettes a day, compared with 43.4% of the controls).

This observation was confirmed when the data were examined according to place of interview (Tables IV and V). There was very little difference for either males or females between the smoking habits of sanatorium and chest clinic patients or between out-patient and in-patient controls, and both sanatorium and chest clinic patients showed the same excess of heavy smokers and deficiency of light smokers and non-smokers when compared with either of the two control groups.

It has already been mentioned that in the general population the amount smoked is known to vary considerably with age. The possibility has to be considered, therefore, that the observed difference between smoking habits of tuberculous patients and controls may be due at least in part to the fact that the two groups have different age structures. That this is not the explanation is demonstrated in Tables VI and VII. For both sexes there was in each ten-yearly age group a consistent excess of heavy smokers and deficiency of light smokers and non-smokers when compared with the corresponding control group. Age standardization of the smoking habits of patients and controls aged 30 years and over (by applying the observed smoking rates in each ten-yearly age group to a standard population with the age structure of patients and controls combined—Table VIII) indicates that in fact Table III somewhat underestimates the difference. And at this point it is of interest to note that for the age group 20–24 years there was no appreciable difference between the smoking habits of the tuberculous and their controls (Table IX).

There still remains one serious objection to be considered: we have been comparing smoking habits of controls at the present time with smoking habits of a tuberculous population at the time of notification. This might have influenced the result in two ways. First, since tobacco consumption in the United Kingdom is still rising, on the average persons of a given age are likely to be smoking a little more heavily to-day than persons of the same age a few years ago. Clearly this cannot account for the observation that tuberculous patients had smoked more than controls, since they were asked about their smoking habits at a time when tobacco consumption was on the average a little less than it is to-day. Secondly, estimates of amount smoked in the past are likely to be less reliable than estimates of amount smoked at time of interview, and it is possible that this may have resulted in exaggeration of past smoking habits. Table X suggests that this is not so. There was no appreciable difference in estimates of amount smoked at time of notification between patients notified within the twelve months preceding interview and patients notified five or more years earlier.

TABLE VI.—*Smoking Habits of Male Patients and Controls in Ten-yearly Age Groups*

| Age | | No. of Cigarettes Smoked per Day | | | | | | Total |
|---|---|---|---|---|---|---|---|---|
| | | 0 | 1–9 | 10–19 | 20–29 | 30–39 | 40+ | |
| 20–29 | Patients | 13·6 | 16·0 | 39·9 | 20·2 | 4·1 | 6·2 | 100% (243) |
| | Controls | 20·7 | 11·7 | 34·5 | 22·8 | 7·6 | 2·8 | 100% (145) |
| 30–39 | Patients | 4·3 | 7·6 | 39·8 | 28·9 | 11·8 | 7·6 | 100% (211) |
| | Controls | 12·7 | 9·5 | 31·7 | 33·3 | 7·9 | 4·8 | 100% (126) |
| 40–49 | Patients | 1·8 | 7·9 | 38·4 | 25·6 | 12·2 | 14·0 | 99·9% (164) |
| | Controls | 7·1 | 8·5 | 39·7 | 23·4 | 11·3 | 9·9 | 100% (141) |
| 50–59 | Patients | 1·0 | 11·5 | 36·5 | 35·6 | 10 6 | 4·8 | 100% (104) |
| | Controls | 3·9 | 16·5 | 37·9 | 28·2 | 9·7 | 3·9 | 100% (103) |
| 60+ | Patients | — | 17·1 | 31·7 | 31·7 | 7·3 | 12·2 | 100% (41) |
| | Controls | 8·2 | 26·5 | 28·6 | 22·5 | 6·1 | 8·2 | 100% (49) |

TABLE VII.—*Smoking Habits of Female Patients in Ten-yearly Age Groups*

| Age | | No. of Cigarettes Smoked per Day | | | | Total |
|---|---|---|---|---|---|---|
| | | 0 | 1–9 | 10–19 | 20+ | |
| 20–29 | Patients | 45·2 | 28·6 | 21·0 | 5·2 | 100% (252) |
| | Controls | 48·2 | 28·3 | 17·5 | 6·0 | 100% (166) |
| 30–39 | Patients | 35·4 | 23·1 | 32·3 | 9·2 | 100% (130) |
| | Controls | 40·7 | 31·9 | 24·8 | 2·7 | 100% (113) |
| 40–49 | Patients | 30·6 | 16·7 | 33·3 | 19·4 | 100% (36) |
| | Controls | 54·3 | 18·1 | 24·5 | 3·2 | 100% (94) |
| 50+ | Patients | 63·2 | 10·5 | 15·8 | 10·5 | 100% (19) |
| | Controls | 73·8 | 26·2 | — | — | 100% (42) |

TABLE VIII.—*Smoking Habits of Patients and Controls (Aged 30 Years and Over) Standardized for Age Distribution*

| | Males | | | | | | | Females | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | No. of Cigarettes Smoked per Day | | | | | | Total | No. of Cigarettes Smoked per Day | | | | Total |
| | 0 | 1–9 | 10–19 | 20–29 | 30–39 | 40+ | | 0 | 1–9 | 10–19 | 20+ | |
| Patients .. | 2·3 | 9·5 | 37·8 | 29·6 | 11·2 | 9·5 | 100% | 37·9 | 19·4 | 30·3 | 12·4 | 100% |
| Controls .. | 8·5 | 12·3 | 35·4 | 27·9 | 9·2 | 6·6 | 100% | 49·5 | 27·0 | 21·2 | 2·5 | 100% |

TABLE IX.—*Smoking Habits of Patients and Controls Aged 20–24 Years*

| | Males | | | | | | | Females | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | No. of Cigarettes Smoked per Day | | | | | | Total | No. of Cigarettes Smoked per Day | | | | Total |
| | 0 | 1–9 | 10–19 | 20–29 | 30–39 | 40+ | | 0 | 1–9 | 10–19 | 20+ | |
| Patients .. | 23·9 (26) | 14·7 (16) | 41·3 (45) | 12·8 (14) | 3·7 (4) | 3·7 (4) | 100% (109) | 51·9 (69) | 23·3 (31) | 21·1 (28) | 3·8 (5) | 100% (133) |
| Controls .. | 23·0 (17) | 10·8 (8) | 36·5 (27) | 23·0 (17) | 5·4 (4) | 1·4 (1) | 100% (74) | 60·7 (51) | 23·8 (20) | 11·9 (10) | 3·6 (3) | 100% (84) |

Males: $\chi^2_4=2{\cdot}5$; $0{\cdot}7<P<0{\cdot}5$. (All males smoking 30 or more cigarettes a day grouped together.)
Females: $\chi^2_3=2{\cdot}8$; $0{\cdot}3<P<0{\cdot}2$. (All females smoking 10 or more cigarettes a day grouped together.)

TABLE X.—*Smoking Habits of Males Aged 30 Years and Over Related to Interval Since Notification*

| Years Since Notification | No. of Cigarettes Smoked per Day | | | | | | Total |
|---|---|---|---|---|---|---|---|
| | 0 | 1–9 | 10–19 | 20–29 | 30–39 | 40+ | |
| 0 .. | 2·9 | 10·9 | 38·5 | 27·5 | 12·1 | 8·0 | 100% (174) |
| 1–2 .. | 1·2 | 8·0 | 40·1 | 29·6 | 11·7 | 9·3 | 100% (162) |
| 3–4 .. | 2·4 | 8·5 | 34·1 | 35·4 | 8·5 | 11·0 | 100% (82) |
| 5 and over | 3·9 | 8·8 | 37·3 | 27·5 | 11·8 | 10·8 | 100% (102) |

## Discussion

If the control group is representative of the local population from which the tuberculous patients were drawn, and there is no reason to doubt this, there appears to be a direct association between smoking habits and respiratory tuberculosis in adults. The interpretation of this observation is another matter, and it is hardly necessary to point out that although such an association suggests that the amount of tobacco smoked may play a part in determining whether a healed or quiescent pulmonary lesion breaks down, it does not and can never prove it. We must inquire whether the hypothesis is consistent with our knowledge of respiratory tuberculosis and of the history of smoking.

In the past it has been generally accepted that the high death rate among middle-aged and elderly males indicates a high attack rate, and consequently in the search for an explanation attention had been focused upon the opportunities for infection (or reinfection) offered by working conditions in highly industrialized communities. Recently serial mass *x*-ray examination of a group of people has shown that in both sexes attack rates are highest in young adult life and decline rapidly with increasing age (Springett, 1951), and the discrepancy between high mortality and low attack rates in elderly males suggests that "tuberculosis deaths in later life are usually, though not always, the result of disease acquired many years earlier" (Springett, 1952). This is supported by the analysis of Birmingham notification data already referred to (Lowe, 1954). The notification peak in young adult life (shown graphically in Fig. 2) was almost entirely due to early (group I) disease, while the second peak exhibited by males in late life was predominantly made up of advanced (Group III) disease. To solve the problem of the sex difference it now seems that we have to ask not what conditions are likely to provide opportunity for infection but what influences can precipitate the breakdown of healed or quiescent lesions. General influences (such as faulty nutrition and physical or mental stress) which affect the sexes more or less equally are unlikely to be of great importance, and tobacco smoke is probably the commonest lung irritant with a marked sex differential. And since tuberculosis in young adults is principally a consequence of new infection rather than of breakdown of old disease, if our hypothesis is true we should expect to find no difference between the smoking habits of young tuberculous patients and the population from which they were drawn. Table IX indicates that this is so.

If it is true that smoking can lead to the breakdown of old lesions, it is still not possible from the data available to say whether it is the principal reason for the sex difference in mortality and morbidity in middle and late life. There are, however, two indications that this may be so. First, smoking is still essentially a male habit. Not only are there far fewer non-smokers among males (over 30 years of age 8.1% of male and 51.4% of female controls were non-smokers—Table III), but also among smokers males smoke much more heavily than females (49.9% of male and 5.0% of female smokers had smoked 20 or more cigarettes a day). Second, the difference in amount smoked between patients with respiratory tuberculosis and controls in this investigation is similar to the difference between patients with cancer of the lung and their controls reported by Doll and Hill (1952). For both males and females there is a similar deficiency of non-smokers and light smokers and an excess of moderate and heavy smokers. In England and Wales during the quinquennium 1950–4 the ratio of male to female deaths from cancer of the lung was 6:1, while for respiratory tuberculosis at age 55 years and over it was 5:1.

Finally, we must consider whether what is known about the growth of the tobacco habit in this country and the changing pattern of tuberculosis in middle life is consistent with the suggestion that there may be a causal relationship between them. Tobacco consumption in the United Kingdom began to rise steeply shortly after the 1914–18 war, and it was during the decade 1921–30 that a rapid increase in mortality attributed to cancer of the lung first began to attract attention (Doll and Hill, 1950). No great weight can be attached to this relationship, since, as has so often been pointed out, a substantial part of the increase in mortality from cancer of the lung is probably due to improved diagnosis and more accurate death certification. In the case of respiratory tuberculosis a direct comparison between mortality and tobacco consumption is even less instructive, because death rates have always provided a very unreliable measure of incidence, and in recent years therapeutic advances have profoundly altered the pattern of survival. Since our principal concern is with the change in sex pattern of tuberculosis in middle life it is possible to side-step these difficulties. In Fig. 4, which illustrates changes in the ratio of male to female death rates for various age groups over the past hundred years (a method used by Springett, 1952), a rising ratio indicates that the male death rate is declining less rapidly than the corresponding female death rate, and vice-versa. It is evident that in the age group "45 years and over" male mortality has been declining less rapidly than female mortality for at least a century, but since 1911–20 (the decade in which tobacco consumption began to climb) the sex difference has become very much more pronounced.

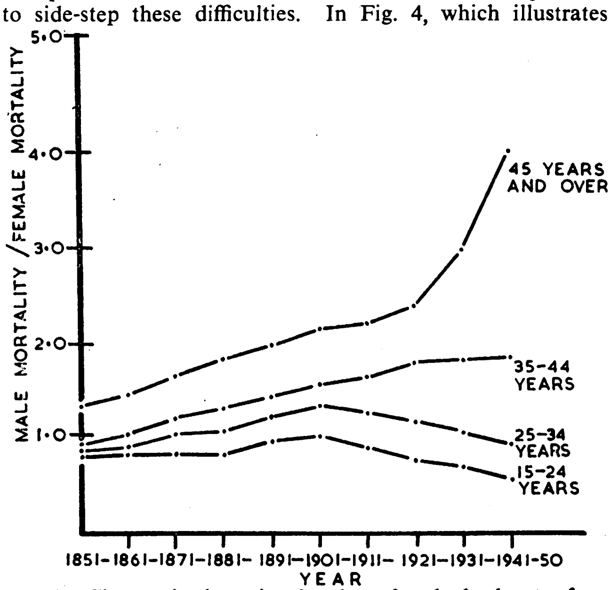

FIG. 4.—Changes in the ratio of male to female death rates from respiratory tuberculosis in certain age groups from 1851.

It seems reasonable to conclude that smoking may be an important cause of the breakdown of healed or quiescent respiratory tuberculosis in middle and late life and perhaps the principal reason for the rapidly increasing sex difference in mortality at these ages.

## Summary

No satisfactory explanation has been provided for the observation that in most large industrialized countries mortality from respiratory tuberculosis in middle and late life is now very much higher for males than for females. In view of the association between smoking and cancer of the lung, in which male mortality is also relatively high, it was decided to investigate the smoking habits of patients with respiratory tuberculosis.

A social worker questioned 1,200 patients with notified respiratory tuberculosis about their present and past smoking habits: 766 were interviewed at the Birmingham Chest Clinic and 434 in the three principal Birmingham sanatoria. The same worker interviewed as controls 588 patients attending the Birmingham Accident Hospital with minor injuries and 391 patients occupying beds in the surgical wards of a large non-teaching hospital in Birmingham.

In both sexes patients of over 30 years of age with respiratory tuberculosis showed a highly significant deficiency of non-smokers and light smokers and an excess of moderate and heavy smokers when compared with the controls. It seems unlikely that this difference is due to a bias in choice of patients and controls or to the method of comparison.

From this and from certain other considerations it is suggested that smoking may be an important cause of the breakdown of healed or quiescent respiratory tuberculosis in adults and may account for a considerable part of the excessive male mortality in middle and late life.

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# LATE RESULTS OF VAGOTOMY COMBINED WITH GASTRO-JEJUNOSTOMY OR PYLOROPLASTY IN THE TREATMENT OF DUODENAL ULCERATION

BY

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Sedation, diet, antacids, and antispasmodics have long been accepted in the medical treatment of duodenal ulceration. There is, however, no equivalent unanimous surgical opinion regarding the most satisfactory operative procedure, for the functional result achieved has to be evaluated in conjunction with the incidence of recurrent or stomal ulceration.

Vagal nerve section, reintroduced by Dragstedt *et al.* (1944), soon fell into disrepute for duodenal ulceration because of the high incidence of gastric retention, with all its sequelae, which followed this operation. The addition of gastro-jejunostomy or pyloroplasty as a simultaneous procedure has materially diminished the frequency of this delay in stomach emptying. Nevertheless, both these gastric drainage procedures have complications peculiar to themselves. Particularly is this so with gastro-jejunostomy, in which both the liability of the stomach region to peptic ulceration and also the production of symptoms by mechanical factors or by the regurgitation of duodenal juice have long been appreciated.

## Present Series

In this paper are embodied the results of an analysis of 366 cases of chronic duodenal ulceration treated by vagotomy combined with either gastro-jejunostomy or pyloroplasty. The length of time post-operatively has been five years or longer in most cases. The series consists of consecutive cases drawn from several surgical centres in this country. In this way it is thought to be representative of the overall late results obtained in current surgical practice by these operations.

Out of this complete group, 22 (6%) patients had died from causes unconnected with their duodenal ulceration, and 14 (3.8%) have been lost, leaving 330 (297 males, 33 females) for study. In all cases section of the vagi was performed transabdominally, the nerves being exposed on the lower oesophagus after mobilization of the left lobe of the liver. Pyloroplasty was carried out in most cases by the method of Heineke–Mikulicz, which consists of enlargement of the pyloric opening by an incision parallel to the long axis of the stomach and closure of this by suture at right angles to the original incision. In other patients the method of combined pyloroplasty and pylorectomy advocated by Beattie (1950) was employed. All operations were elective, none being for the emergency treatment of haemorrhage or perforation. In all cases the clinical and radiological diagnosis of duodenal ulceration was confirmed at operation.

Follow-up has been by personal visit to the patient's home in 37 cases (10.2%), out-patient review of 120 cases (36.4%), and by questionary in 173 cases (53.4%). The questionary covered the following points: (*a*) the extent of the patient's satisfaction with the operative result; (*b*) any return of ulcer pain; (*c*) any further stomach operations; (*d*) any post-operative haematemesis or melaena; (*e*) a survey of the possible post-operative symptoms; and (*f*) weight gain or loss since operation. In any case where there was doubt the patient was seen or the position made clear by further correspondence.

The length of time since operation was four years in 52 (15.8%) cases, five years in 219 (66.4%), six years in 51 (15.4%), and seven years in 8 (2.4%).

The operative procedure in 198 cases (60%) was vagotomy and gastro-jejunostomy, and in 132 cases (40%) it was vagotomy and pyloroplasty.

## Clinical Results

The results of the review have been classified in general accordance with the method of Visick (1948). Separation has been made into the following groups:

*Grade I: Patients Who are Completely Symptom-free.*—There were 167 cases (50.6%) in this grade. With the complete absence of subjective or objective troubles, the excellence of the result obtained leaves nothing to discuss.

*Grade II: Patients Who Have Mild Symptoms which Cause No Disability.*—There were 113 cases (34.2%) in this grade. It must be emphasized that the symptoms complained of were minor and did not detract from the good operative result, either in the patients' or the reviewer's opinion. They occurred so infrequently in the majority that it was only the rigid adherence to the complete absence of symptoms necessary for classification in grade I that prevented their inclusion in this latter grade. The complaints were of