G.P.I. There were a relatively large number of negative Wassermann reactions in both blood and C.S.F. in meningo-vascular syphilis, and certainly more (8%) than were expected in G.P.I. There was also 8% of cases of G.P.I. in which, although the blood Wassermann reaction was positive, the C.S.F. Wassermann reaction was negative. This is unexpected, as it is usually thought that the Wassermann reaction is almost always positive in the C.S.F. The wide variations in the findings in congenital syphilis were not unexpected.

Other Neurological Disorders

The findings in some other neurological disorders investigated were in general agreement with those already published in standard textbooks, but one or two points might be mentioned. The C.S.F.s from 29 patients with a cerebral abscess have been examined, and only seven of them were even faintly turbid. In eight the cell count was normal, while, of the remainder, 13 showed between 5 and 100 cells; polymorphonuclear leucocytes were seen in only 19 of the 29 fluids. The protein was normal on 10 occasions and less than 200 mg./100 ml. in all except three fluids. No other significant features were noted.

Fluids from 10 patients with a cerebral tuberculoma diagnosed during life were examined, and all seven who died were seen in the pre-streptomycin era. The only significant features that emerged from the examinations made in this very small series was that the pre-operative fluid may contain neither an increased cell count nor a raised protein content.

Many other comments could be made, but the evidence for these is slight; one remark can, however, be added—namely, that there was found to be a rather wider variation in the results than one is commonly inclined to allow; and one lesson that we have personally learned is to be rather less dogmatic than had previously been our custom.

Summary

An analysis of the results obtained from the examination of nearly 12,000 C.S.F.s from various neurological disorders has been made.

The C.S.F. in 835 cases of all types of cerebral tumour has shown a cell increase in only 8.3% of cases, but a protein increase in 71.1%, cerebral glioma giving figures of 10.7% and 66.5% respectively. Fluids from cases of neurofibromata—whether on the fifth or the eighth cranial nerve—contained a protein content raised above the normal.

In 6.1% of the cases of epilepsy the fluid protein was raised above 70 mg./100 ml., and in two cases a figure of over 100 mg./100 ml. was obtained.

The findings in 690 patients with multiple sclerosis are discussed, and in 1.9% of cases—many verified at necropsy—there was a protein content in the fluid above 150 mg./100 ml.

Unexpected results were not found in subacute combined degeneration, diabetic neuritis, infective polyneuritis, syringomyelia, or subdural haematoma.

The results of fluid examination in 238 cases of spinal tumour were in conformity with previous reports, but figures for protein as high as 4,000 mg./100 ml. were found.

The cases of neurosyphilis examined (770) are fewer than expected, but the findings, apart from the results of the Lange and Wassermann tests, were similar to those previously recorded. The most unexpected finding was an occasional negative fluid Wassermann reaction in G.P.I.

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BRONCHITIS MORTALITY RATES IN ENGLAND AND WALES AND IN DENMARK

BY

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In England and Wales bronchitis is recorded as the cause of death in over 25,000 people every year, and it accounts for half the deaths due to respiratory diseases and 5% of deaths due to all causes. The recorded mortality rates in other European countries and in the United States of America are much lower. In this paper the causes of death in England and Wales and in Denmark are analysed and compared, and some factors are considered which might be responsible for the recorded excess mortality from bronchitis in England and Wales.

The difference in mortality rates for bronchitis in the two countries obtained from the Registrar-General's Statistical Review and the Causes of Death in the Kingdom of Denmark is shown in Fig. 1.

FIG. 1.—Mortality rates per 100,000 from bronchitis in England and Wales (E. & W.) and in Denmark: average for 1951–5. Bronchitis includes: acute bronchitis (500); bronchitis, unqualified (501); chronic bronchitis (502), including bronchitis with emphysema (502.0) and other (502.1). The International List numbers are given in parentheses.

Choice of Cause of Death from Death Certificates

The current form of death certificate used in England and Wales, which has space for recording the underlying cause, complications, and contributory causes, was introduced in 1927. For thirteen years the selection of the cause of death for tabulation from certificates giving multiple causes was governed by a set of rules which gave priority to certain causes. For example, any definite disease of the kidneys or heart (and this included myocardial degeneration) was preferred to any respiratory disease. In 1940 the International Statistical Classification of Diseases, Injuries, and Causes of Death was adopted, and this lays down that, with certain exceptions, the cause of death for tabulation shall be that which the certifier records as the underlying cause.

The effect of this change in selection procedure on bronchitis mortality rates for men in England and Wales in 1939 was calculated by Schilling and Goodman (1951). They found that by applying the 1940 method of classification to the 1939 figures it increased the age specific mortality rates from bronchitis by the following amounts: 25–34 years, 31%; 35–44 years, 48%; 45–54 years, 71%; 55–64 years, 97%; and 65–69 years, 114%.

Since 1951 Denmark has also used both the International Certificate of Cause of Death and the International Statistical Classification of Diseases, Injuries, and Causes of

Death, but for chronic bronchitis the special rules given below are applied (Lindhardt—personal communication):

1. Whenever chronic bronchitis appears together with arteriosclerotic heart disease, including coronary disease (420), other myocardial degeneration (422), functional disease of heart (433), and other and unspecified diseases of heart (434), they—the heart diseases—will be coded as the underlying cause.

2. Whenever chronic bronchitis appears together with bronchiectasis (526) the latter will be coded as the underlying cause; whenever chronic bronchitis appears together with lobar pneumonia (490) the latter will be coded as the underlying cause.

3. Chronic bronchitis together with asthma bronchiale (241) is coded as chronic bronchitis (502) unless the patient died in status asthmaticus.

4. Until 1955 chronic bronchitis together with bronchopneumonia was coded as bronchopneumonia (491), but now this combination is coded as chronic bronchitis (502).

These Danish rules, which are in essence the same as those used in England and Wales before 1940, would only have the effect of reducing the bronchitis mortality rates if another cause of death was often combined with chronic bronchitis. The analysis of multiple causes of death which was undertaken by the Registrar-General on a sample of death certificates in 1951 (Registrar-General, 1951) shows that bronchitis often occurs in combination with other diagnoses. If the Danish rules of selection are applied to this sample of English certificates many cases tabulated as chronic bronchitis would be ascribed to cardiovascular causes. This would reduce the total bronchitis mortality rate of this sample by approximately 45%. The same procedure cannot be applied to Danish death certificates because multiple causes of death are not tabulated, but the death rates from causes to which cases of bronchitis in Denmark might be ascribed according to their rules are given in Table I with the corresponding rates for England and Wales.

TABLE I.—*Crude Mortality Rates per 100,000 (Both Sexes, 1954) for Various Groups of Diseases to which Cases of Bronchitis Might be Ascribed in Denmark, Compared with Rates in England and Wales*

Causes of Death	International Number	Crude Death Rate	
		England and Wales (Pop. 44,274,000)	Denmark (Pop. 4,405,700)
Acute bronchitis	500	7	2
Bronchitis, unqualified ..	501	5	0
Chronic bronchitis	502	46	4
Asthma bronchiale	241	6	1
Arteriosclerotic heart disease, including coronary disease ..	420	151	150
Other myocardial degeneration ..	422	145	50
Functional disease of heart ..	433	6	6
Other and unspecified diseases of heart	434	11	28
Lobar pneumonia	490	7	3
Bronchopneumonia	491	30	15
Bronchiectasis	526	4	2
Total		418	261

There is an excess mortality in England and Wales for all the respiratory and cardiac conditions recorded in Table I, except "Other and unspecified disease of heart" (434). Even if the whole of the Danish excess in this group were due to differences in the diagnosis and assignment of cases of bronchitis, which is unlikely, it could not explain the tenfold excess in bronchitis mortality in England and Wales.

In contrast to the large difference in mortality from chronic bronchitis, there is a marked similarity in the rates for diseases, such as congenital malformations and neoplasms, in which a greater uniformity of diagnostic habit is to be expected (Table II).

It is likely that the different death rates for the two countries cannot be explained wholly by different methods of bookkeeping and that there is a real excess of deaths from chronic bronchitis in England and Wales. Some causes of this excess are considered.

TABLE II.—*Crude Death Rates per 100,000 (Both Sexes, 1954) in Certain Groups of Diseases in England and Wales and in Denmark*

Causes of Death	International Number	Crude Death Rate	
		England and Wales	Denmark
Neoplasms	140-239	207	198
Diseases of the genito-urinary system	590-637	28	31
Diseases and complications of pregnancy, childbirth, and the puerperium ..	640-689	5*	6*
Congenital malformations ..	750-759	10	9

* Rates per 100,000 women aged 15-44.

Age and Sex.—The greater number of deaths from bronchitis in England and Wales is not due to difference in age and sex distribution. Of the deaths from chronic bronchitis, 95% occur over the age of 45. In England and Wales this age group comprises 36% of the total population, compared with 32% in Denmark, and 47% are male compared with 48% in Denmark. The age specific death rates for males and females in the two countries (Table III) show that the

TABLE III.—*Age and Sex Specific Death Rates per 100,000 (1954) for Chronic Bronchitis (502)*

Age	Population in 1,000's		Total Deaths		Death Rate	
	E. and W.	Denmark	E. and W.	Denmark	E. and W.	Denmark
<i>Males</i>						
0-14	5,092	600	21	2	0	0
15-44	9,002	909	200	4	2	0
45-54	3,863	274	1,204	8	39	3
55-64	2,106	205	3,437	20	163	10
65-74	1,380	134	5,331	23	386	17
75+	645	65	4,374	48	678	74
<i>Females</i>						
0-14	4,863	571	14	0	0	0
15-44	9,236	915	74	3	1	0
45-54	3,222	285	245	2	8	1
55-64	2,633	223	683	10	26	4
65-74	1,948	149	1,708	13	88	9
75+	1,084	74	2,995	53	76	71

excess mortality in England and Wales occurs at all ages for both sexes. It will also be seen that the great predominance of male deaths in England and Wales is much less marked in Denmark.

Social Class.—The social-class gradient of mortality from chronic bronchitis in this country cannot be compared directly with Danish figures, as these are not broken down by social class. However, a comparison, related to social class, can be made in the level and distribution of the national income per head (United Nations, 1952). In both countries the average income is within the range of U.S. \$600-699 and the distribution is about the same. The proportion of the total national income received by the richest tenth in the United Kingdom (after income tax) is 26% and in Denmark 29%. The proportion of the total received by the poorest half in the United Kingdom is 30%, compared with 23% in Denmark. Thus it is unlikely that differences in the standard of living are a major factor in the different bronchitis mortality rates.

Urban and Rural Residence.—The mortality rates from bronchitis according to residence are shown in Table IV. In England and Wales the well-known urban-rural gradient in bronchitis mortality is clearly shown. In the Danish figures there is, by contrast, a slightly higher mortality in the rural districts. Air pollution has been suggested as one factor responsible for the urban-rural gradient in England and Wales. Campbell and Clemmesen (1956) made a comparative study of air pollution in the two countries and concluded that Copenhagen, the most industrialized city in Denmark, was polluted to about the same extent as an English rural town. However, from Table IV it will be seen that the mortality rates for bronchitis in all areas in Denmark are lower than for rural districts in England and Wales. It is therefore unlikely that the difference in the mortality rates could be due to differences in air pollution alone.

TABLE IV.—Crude Death Rates per 100,000 (Both Sexes, 1954) from Bronchitis (500-502) by Residence

England and Wales			Denmark		
Regions	Population in 1,000's	Death Rate	Regions	Population in 1,000's	Death Rate
Conurbations . . .	16,894	65	Copenhagen . .	776	6
Urban area with population of 100,000 and over	5,851	61	Provincial towns, including Frederiksberg	1,292	5
Urban area with population of 50,000 and under 100,000	3,391	58	Rural districts, including Gentofte	2,357	7
Rural districts . .	8,610	42			

Tobacco Consumption.—A comparison of the average weight of tobacco consumed per head per year in England and Wales and in Denmark, and the proportion of this that is smoked as cigarettes, are given in Fig. 2. The total annual

FIG. 2.—Tobacco consumption in England and Wales (—) and Denmark (---), 1905-55. Left: Total annual consumption of tobacco (unmanufactured) per person, in pounds. Right: annual tobacco consumption as cigarettes per person, in pounds.

consumption per head has been lower in this country than in Denmark except for the war years. However, the amount smoked as cigarettes has always been more than twice the Danish figures. Oswald *et al.* (1953), Palmer (1954), and Ogilvie and Newell (1957) have shown that the prevalence of bronchitic symptoms is related to cigarette-smoking. The national smoking habits may therefore contribute to the bronchitis mortality excess recorded in England and Wales.

Climatic Conditions.—In England and Wales the mean annual rainfall is a little greater than in Denmark and the winter temperatures are a little higher. However, both countries lie in the same belts of mean annual temperature (7.22-10.00° C.), mean atmospheric pressure (754.4-759.5 mm.), and wind direction. Thus climate alone cannot directly contribute to the excess in England and Wales.

Summary and Conclusion

A fifteenfold excess of mortality from bronchitis is recorded in England and Wales compared with Denmark. Both countries use the International Certificate of Cause of Death and the International Statistical Classification of Diseases, Injuries, and Causes of Death. However, differences in the method of selecting causes of death for statistical purposes, when multiple causes are given, still occur: these could account for as much as half the excess mortality in England and Wales. Possible differences in diagnostic habits may contribute to the remaining excess but do not appear to explain it. The cigarette consumption of England and Wales is twice that of Denmark and might also contribute to this excess; but when considered separately the differences in the age distribution, social class, climate, and atmosphere pollution of the two countries do not appear to be important factors.

Within the strict limits imposed by differences in method of compiling the death rates, it would appear that there is a real excess of the disease labelled bronchitis in England and Wales, compared with Denmark; but the confirmation of this difference and the elucidation of its causes are likely to result only from comparative field surveys in the two countries.

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ANTIBODY RESPONSES TO BRITISH POLIOMYELITIS VACCINE OF CHILDREN WITH NATURALLY OCCURRING ANTIBODY

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The results have already been reported of a study of the antigenic activity of British poliomyelitis vaccine in a group of children who, at the time of their first injection of vaccine, had no antibodies to any of the three types of poliomyelitis virus (Medical Research Council, 1957a). In selecting this group the sera of a number of children in five different areas were tested, and, although those who were shown to have antibodies to one or more types were excluded from the Council's study, they were nevertheless injected with poliomyelitis vaccine. The antibody responses of some of these children were investigated and the results are reported here.

Titration of Sera

Sera from 254 London and Manchester children, aged from 1 to 9 years, were obtained before giving two intramuscular injections of formalinized poliomyelitis vaccine (Glaxo) four weeks apart. Samples of sera were also obtained 14 days after the second injection. All sera were titrated for neutralizing antibody to the three types of poliomyelitis virus by the method used routinely in the Biological Standards Control Laboratory (Medical Research Council, 1957a). In this method, serum-virus mixtures are held at 37° C. for three hours before being added to cultures of monkey-kidney cells, and the titres (PD₅₀) expressed as the dilution of serum in the serum-virus mixture and not as the initial serum dilution. The three virus strains used in the neutralization tests were the same as those employed in the manufacture of British vaccine—namely, the attenuated Brunenders for type 1, MEF-1 for type 2, and Saukett for type 3. In three cases one type was omitted because of insufficient serum. Children whose serum at a dilution of 1/8 did not inhibit any one of the poliomyelitis viruses were regarded as negative so far as that type was concerned. The sera of those who did not produce this titre after vaccination were also tested at a dilution of 1/4.