Papers and Originals

Burden of Cerebrovascular Disease in the Oxford Area in 1963 and 1964

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Summary: The only available information on the magnitude of the problem of cerebrovascular disease in England and Wales is to be found in the mortality data of the Registrar General and in the Hospital Inpatient Enquiry, which enumerates spells of illness but not the people suffering from those spells. There are no representative morbidity statistics. Data collected by the Oxford Record Linkage Study show that in 1963 from a population of 340,000 there were 427 hospital admissions among 391 patients. Of these, 34·5% were aged less than 65 years, and when patients who died at home without having entered hospital were added this figure fell to 26·7%.

The survival rates at one month and one year for all strokes in the community were 43 and 30%, respectively. Married men were found to spend an average of 37 days in hospital, compared with 55 for married women; single women stayed in hospital an average of 10 days longer than single men. It is hoped that in addition to any value the overall findings may have in the planning of health services they will serve as a useful baseline in the evaluation of new methods of prophylaxis and treatment for cerebrovascular disease.

Introduction

It is well known that cerebrovascular diseases impose a heavy burden on the community. The evidence most frequently cited in support of this statement is provided by mortality data. For instance, in England and Wales in 1963 and 1964 157,074 persons are recorded as having died of cerebrovascular disease, 19·9% of them being under the age of 65 years (General Register Office, 1965, 1966). These stroke deaths represent 14·2% of all the deaths in the community in those two years. Another source of information, less generally quoted, is the Hospital Inpatient Enquiry conducted jointly by the Ministry of Health and the General Register Office (1967, 1968). This shows that in the same years, 1963 and 1964, there were 150,409 discharges from, or deaths in, hospital of patients with cerebrovascular disease—some 7,000 fewer than the total deaths despite the fact that an unknown proportion of the persons discharged were admitted to hospital more than once in a year.

Two other interesting differences between these two sets of figures are that as many as 34% of the hospital discharges alive and dead were in patients under 65 years, but that the entire group with cerebrovascular disease represent only 1·8% of the 8·5 million hospital deaths and discharges in 1963 and 1964. This last fact is not surprising, because (fortunately) far more people are discharged from hospital alive than die in them. The former is, however, intriguing because it indicates both that mortality data may underestimate the magnitude of the problem caused by cerebrovascular diseases among middle-aged people, and that a considerable number of old people must die of cerebrovascular disease without ever getting to hospital. This is conjecture, however, partly because we have no information at all about the true incidence of cerebrovascular accidents in the country, and partly because at the moment the Hospital Inpatient Enquiry can give information only about episodes of illness and not about the people who suffer those episodes.

Theoretically the procedures involved in record linkage can overcome these difficulties completely provided that all the relevant health information about each person in the community is included in the file—records from general practice, hospital outpatient data, hospital inpatient data, and death certificates. In 1963 and 1964 the Oxford Record Linkage Study did not include information from the first two sources, but obtained complete records from the last two. The purpose of this paper is to present an attempt based on the techniques of record linkage to assess the burden of cerebrovascular disease among the 340,000 people included in the Oxford Record Linkage Study in terms of estimated incidence, mortality, estimated survival rates, and bed usage. Not only is such information of value in the planning of health services, but it also can serve as a useful baseline for the long-term evaluation of treatment with such agents as anticoagulants and hypotensive drugs.

Subjects and Methods

Full details of the origin of the Oxford Record Linkage Study and the techniques it uses are given elsewhere (Acheson, 1967). The population it considers is similar in size to that of Oxfordshire, though it is not wholly coincident with it, including as it does some people who live in Berkshire and excluding a few in Oxfordshire. All hospitals in the area submit to the Study information about every discharge and death occurring in them; data include demographic and medical details, among which are the diagnoses that have been made. Copies of all death certificates relating to the population, including those of persons dying outside the area, are supplied by the Registrar General. The Registrar General does not publish annual population estimates by age for the local administrative areas of the Oxford Record Linkage Study. Estimates by age and sex of the population of the Study area have therefore been made by subdividing the total population at all ages, published for each sex, in proportions derived from the 1961 Census data. These estimates for 1963 are given in Table I.

This paper is concerned with people whose records were coded under one of the following rubrics of the seventh revision of the International Classification of Disease (I.C.D.): 330 (subarachnoid haemorrhage), 331 (cerebral haemorrhage), 332 (infarction due to cerebral thrombosis and/or embolism),

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TABLE I.—*Persons Treated in Hospital for Cerebrovascular Disease in the Oxford Record Linkage Study Area in* 1963 *by Age, Sex, and I.C.D. Category per* 1,000 *Population at Risk.*

Age in Years	Males						Females					
	Population at Risk	I.C.D. Codes					Population at Risk	I.C.D. Codes				
		330	331	332	334	330–334		330	331	332	334	330–334
⩽34	94,981	0·02	—	—	0·02	0·04	84,045	0·01	—	—	0·01	0·02
35 –	21,902	0·05	—	0·05	—	0·10	22,042	0·14	0·04	—	—	0·18
45 –	22,293	0·13	0·18	0·22	0·22	0·75	22,488	0·36	0·13	0·18	0·13	0·80
55 –	16,992	0·29	0·82	0·71	0·88	2·70	18,221	0·55	0·93	0·49	0·33	2·30
65 –	9,177	0·32	2·15	1·72	0·54	4·73	13,679	0·29	1·90	1·68	1·02	4·89
75+	4,902	0	3·26	4·90	3·47	11·63	8,788	0·57	3·30	3·41	2·73	10·01

334 (other and ill-defined forms of cerebrovascular disease)—there were no cases coded as 333. Records included were either death certificates of people who died in 1963 and bore an entry coded 330-334 as the underlying cause of death, or people who were discharged from hospital in 1963 with such a code. In order to obtain one-year survival information the 1963 hospital records for this latter group were linked with certificates of death occurring within 12 months of hospital discharge, including, therefore, some death certificates for 1964. Among those who died no attempt was made to distinguish between those whose death was ascribed to cerebrovascular disease and those who were recorded as having died of other causes.

Results

Hospital Data

In Table I the 391 persons treated in hospital for cerebrovascular disease in 1963 in the Oxford Record Linkage Study area are presented by age, sex, and I.C.D. category in the form of rates, as the numbers of persons affected per thousand persons at risk. There were 427 admissions in all during the calendar year 1963 among the 391 people whose case records bore the hospital diagnosis of stroke; 34·5% of them (40·6% of the men and 29·9% of the women) were aged less than 65 years. It can be seen that with the exception of subarachnoid haemorrhage the incidence increases with age in all the categories considered. For subarachnoid haemorrhage (330) the rates are higher in women. For infarction and the non-specific category (332 and 334) the opposite is true. Cerebral haemorrhage (331) shows little sex difference in incidence.

Examination by diagnosis of the survival of these patients led to two general observations. First, even in those patients who survived the original event, less than half live for a year after their admission to hospital, and, second, in general men seem to survive cerebrovascular accidents better than women, especially if the accident is coded as cerebral haemorrhage (331) or cerebral infarct (332). The striking exception to this generalization is subarachnoid haemorrhage (330). This is a commoner reason for admission to hospital of women than of men, but only 43% of the men survived for one month compared with 61% of the women, though the mean age of the men was 55 years and of the women 61 years.

Basis for Assumptions

Comparison between the cases presented in Table I and death certificates in the Oxford Record Linkage Study area indicated that 239 people died at home during 1963 either without having been in hospital at all during that year, or if they had been in hospital their case records did not bear the diagnosis of cerebrovascular disease. The existence of these cases would suggest that the rates presented in Table I are an underestimate of the true incidence. In addition to this group, which would be missed in an analysis based wholly on hospital discharges (live and dead), there is the group of patients diagnosed as suffering from cerebrovascular disease by their general practitioner or as a hospital outpatient and who did not die of this disease. No information is at present available about this group, so that it must be ignored.

Two other sources of discrepancy between hospital data and mortality data must be considered; some of the people who were treated in hospital for stroke in 1963 or 1964 may, in one of those years, have died from some other certified cause, and on the contrary some of those certified as having died in hospital in 1963 or 1964 from stroke may have been treated for another condition. By either method of identification about one-third of the cases underwent a change of diagnosis between cerebrovascular disease (330-334) and some quite different disease category. But, in general, support was found for the often-repeated statement that the gains and losses in mortality data for a lethal condition such as cerebrovascular disease tend to cancel out, so that, provided the standard of medical care and reporting is high, such data give a fair indication of the epidemiology of the disease (Acheson, 1966, 1969; Kurtzke, 1969; etc.). Thus, in addition to the consideration of home deaths from cerebrovascular disease referred to above, a variety of other assumptions or corrections could be made in order to estimate the "true" incidence and survival patterns for the disease in the area.

In arriving at our own working assumptions we used two basic criteria—namely, that they should be (*a*) as simple, and (*b*) as repeatable as possible. The assumptions we have made on this basis are three: (1) for the purpose of calculating estimated total incidence all "home deaths" should be added to the hospital morbidity data shown in Table I; (2) for the purpose of calculating survival "home deaths" should also be treated as incident cases, and it should further be assumed that the reason that they were not admitted to hospital is that they died within one month of the onset of the disease; and (3) for both purposes the gains and losses due to change of diagnosis during the course of the disease cancel each other out and can therefore be ignored.

The third assumption probably leads to an underestimate of true incidence, because, while it is clear that in some cases a change in diagnosis will correct an earlier error, other cases will have genuine multiple diagnoses. The present data do not, however, permit any estimate to be made of the proportions of cases falling in either category, so that the inclusion of such cases in estimates of incidence would involve guesswork and their inclusion in estimates of survival would be impossible. On the other hand, some of the incidents included in this study will be second or subsequent strokes, and it is also impossible to identify them so that their inclusion will inflate the rates.

The numbers of cases provided by the data which use these three assumptions, together with the source, are shown in Table II. The "home deaths" occurred in people with an average age of 76·7 years compared with 69·5 years in the hospital group.

TABLE II.—*Cases of Cerebrovascular Disease in the Oxford Record Linkage Study Area in 1963 by Sex, Source of Information, and I.C.D. Rubric.*

I.C.D. Code	Males			Females			Total
	Hospital* Discharge (Alive or Dead)	"Home† Death"	Both	Hospital* Discharge (Alive or Dead)	"Home† Death"	Both	
330 ..	14	3	17	31	6	37	54
331 ..	54	24	78	76	64	140	218
332 ..	58	55	113	66	72	138	251
334 ..	44	8	52	48	7	55	107
Total ..	170	90	260	221	149	370	630

*Hospital discharge includes all cases in which cerebrovascular disease was a diagnosis on the hospital discharge sheet whether or not, in those who died, this diagnosis was considered to be the underlying cause of death.
†A "home death" in this study is a person who died outside hospital in 1963 from cerebrovascular disease, and who had not been discharged from hospital during that year with that diagnosis.

Estimated Total Incidence and Mortality

The estimated total incidence of strokes is shown by age, sex, and I.C.D. category in Table III and Fig. 1. As is to be expected from our criteria stated above, the incidence rates are higher than those shown in Table I, especially in the older age groups. The overall mortality for the Oxford Record Linkage Study area and the incidence over a 12-month period in 1957-8 in Middlesex County, Connecticut (Eisenberg *et al.*, 1964) are also given in Fig. 1. The proportion of people under 65 years in our study is 26·7%, 31·9% being men and 22·9% women. The incidence rates for cerebral haemorrhage and infarction in Oxford in both sexes tend to be lower than those reported for Middlesex though the overall incidence rates for cerebrovascular disease in the two areas are similar. This point is further discussed below.

TABLE III.—*Estimated Total Incidence of Cerebrovascular Disease in the Oxford Record Linkage Study Area in 1963 by Age, Sex, and I.C.D. Rubric per 1,000 Population.*

Age in Years	Males					Females				
	330	331	331	334	All	330	331	332	334	All
⩽34 ..	0·02	0	0	0·02	0·04	0·01	0·01	0	0·01	0·04
35– ..	0·10	0	0·05	0	0·14	0·14	0·04	0	0	0·18
45– ..	0·13	0·18	0·22	0·22	0·76	0·44	0·22	0·18	0·13	0·98
55– ..	0·41	0·82	1·35	0·88	3·47	0·55	1·43	0·71	0·38	3·07
65– ..	0·32	2·83	3·05	0·65	6·86	0·51	3·00	2·56	1·17	7·24
75+ ..	0	6·94	11·43	4·9	23·27	0·68	7·51	9·78	3·19	21·16

Estimated Overall Survival

The estimated overall survival rates are given in Table IV. If all strokes in the community are taken into account the one-month survival rate is estimated as 43% as compared with 70% in hospital-treated cases, and the one-year survival rate in the total community 30% as compared with 49% for the hospital cases. The community estimates are almost identical with the 43% for one month and 28% for one year reported by Eisenberg *et al.*, (1964) in Middlesex, Connecticut; in both Oxford and Middlesex the average age of all the cases was 72·2 years.

Bed Usage

Facts about bed usage by people discharged from hospital in 1963 or 1964 are given in Table V. This shows that, as might be expected, within each sex the duration of hospital stay is longer in people with infarction (332) than in those with either kind of haemorrhage (330 or 331). There are some interesting contrasts between the sexes. The differences between the duration of stay in persons suffering subarachnoid haemorrhage (330) lends strong support for the findings in

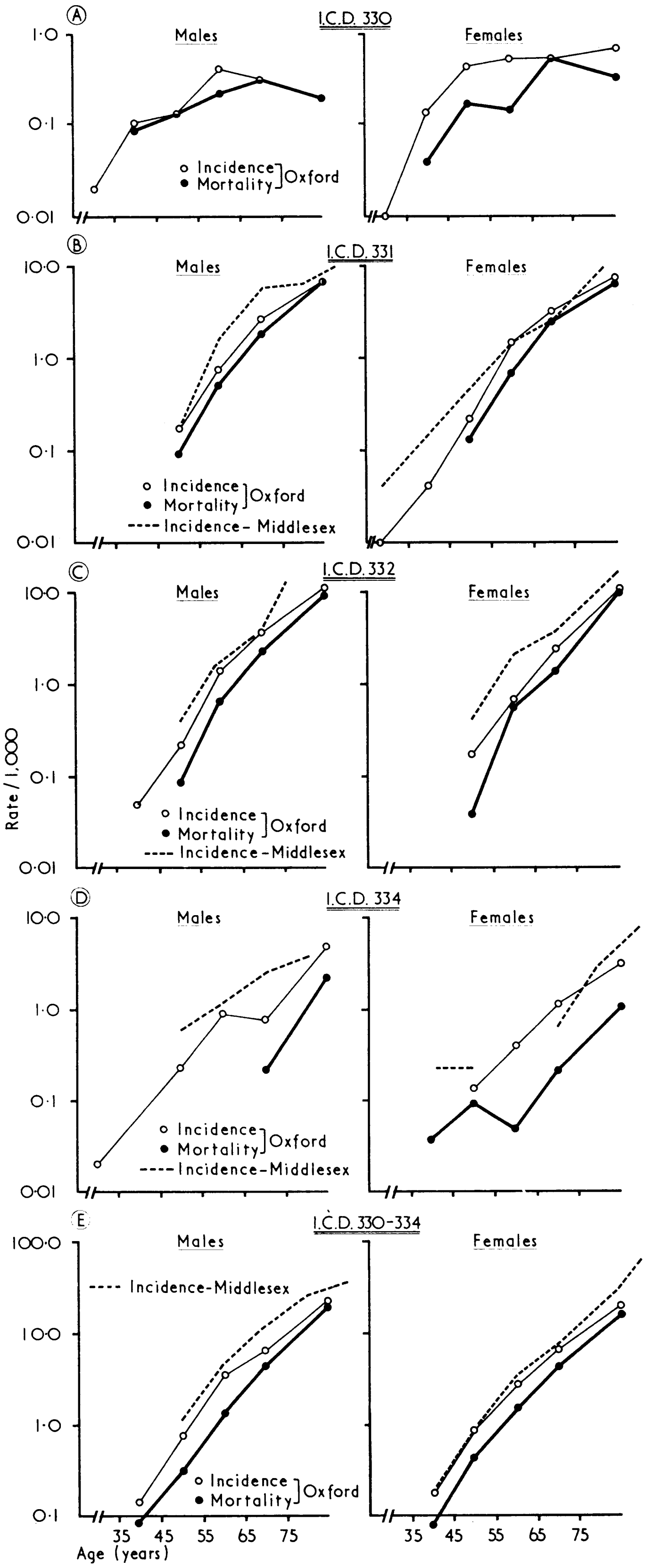

FIG. 1.—Semi-logarithmic plot by age and sex of estimates of incidence and mortality in the Oxford Record Linkage area from the types of cerebrovascular disease recognized by the International Classification of Disease. I.C.D. 330 is subarachnoid haemorrhage (A), 331 cerebral haemorrhage (B), 332 thrombosis and embolism (C), 334 other and unspecified cerebrovascular disease (D), and 330-334 all types of stroke combined (E). The dotted lines (B, C, D, and E) show estimates for Middlesex County, Connecticut for 1957-8 made by Eisenberg *et al.* (1964). Their data for haemorrhage (B) do not differentiate subarachnoid from cerebral haemorrhage and are therefore not strictly comparable with the Oxford data shown in B.

TABLE IV.—*Estimated One-year Survival Rates in Persons Suffering Cerebrovascular Disease in 1963, by Age and Sex*

	No. of Persons	Average Age in Years	% Survival Months 1	6	12
Total	630	72·2	43	35	30
Males:					
≤64 years	83	55·8	65	59	55
65-74 years	63	69·8	49	33	32
≥75 years	114	82·7	33	24	17
All ages	260	71·0	47	37	33
Females:					
≤64 years	85	55·4	57	50	44
65-74 years	99	70·2	47	34	28
≥75 years	186	82·8	30	24	21
All ages	370	73·1	41	32	28
I.C.D. 330:					
Males	17	54·1	35	29	29
Females	37	60·8	51	49	49
Sexes together	54	58·7	46	43	43
I.C.D. 331:					
Males	78	72·4	40	31	28
Females	140	72·8	31	24	21
Sexes together	218	72·7	34	26	23
I.C.D. 332:					
Males	113	73·7	41	32	29
Females	138	76·8	33	24	19
Sexes together	251	75·2	37	27	24
I.C.D. 334:					
Males	52	69·4	77	61	50
Females	55	73·4	78	65	54
Sexes together	107	71·5	78	64	52

TABLE V.—*Hospital Admissions for Cerebrovascular Disease Number of Admissions, Persons Admitted, and Mean Duration of Hospital Stay in 1963 by Age, Sex, and Diagnosis, and in 1963 and 1964 by Marital Status*

Age in Years	Persons Admitted	No. of Admissions	Total Days	Days per Person	Days per Admission
		I.C.D. 330			
Males:					
≤34	2	2	34	17·00	17·00
35–	1	2	25	25·00	12·50
45–	3	3	89	29·67	29·67
55–	5	5	28	5·60	5·60
65+	3	3	19	6·33	6·33
Total all ages	14	15	195	13·93	13·00
Females:					
≤34	1	1	2	2·00	2·00
35–	3	5	60	20·00	12·00
45–	8	9	175	21·88	19·44
55–	10	11	171	17·10	15·55
65+	9	10	1,261	140·11	126·10
Total all ages	31	36	1,669	53·84	46·36
		I.C.D. 331			
Males:					
≤34	—	—	—	—	—
35–	—	—	—	—	—
45–	4	6	305	76·25	50·83
55–	14	15	193	13·79	12·87
65+	38	41	1,420	37·37	34·63
Total all ages	56	62	1,918	34·25	30·94
Females:					
≤34	—	—	—	—	—
35–	1	1	23	23·00	23·00
45–	3	4	81	27·00	20·25
55–	18	19	613	34·06	32·26
65+	56	59	2,080	37·12	35·25
Total all ages	78	83	2,797	35·86	33·70
		I.C.D. 332			
Males:					
≤34	—	—	—	—	—
35–	1	2	19	19·00	9·50
45–	5	6	141	28·20	23·50
55–	12	13	1,924	160·33	148·00
65+	40	44	3,111	77·78	70·70
Total all ages	58	65	5,195	89·57	79·92
Females:					
≤34	—	—	—	—	—
35–	—	—	—	—	—
45–	4	4	40	10·00	10·00
55–	9	9	288	32·00	32·00
65+	53	60	6,223	117·42	103·72
Total all ages	66	73	6,551	99·26	89·74
		I.C.D. 334			
Males:					
≤34	2	2	20	10·00	10·00
35–	—	—	—	—	—
45–	5	5	258	51·60	51·60
55–	15	16	819	54·60	51·19
65+	22	24	2,684	122·00	111·83
Total all ages	44	47	3,781	85·93	80·45
Females:					
≤34	1	1	5	5·00	5·00
35–	—	—	—	—	—
45–	3	3	79	26·33	26·33
55–	6	7	95	15·83	13·57
65+	38	39	3,638	95·74	93·28
Total all ages	48	50	3,817	79·52	76·34

Marital Status. I.C.D. 330-334 (1963 *and* 1964)

Marital Status	No. of Persons	No. of Admissions	Total Days	Days per Person	Days per admission
		I.C.D.	330-334		
Males:					
Not known	14	14	216	15·43	15·43
Single	31	40	2,129	68·68	53·22
Married	223	273	8,164	36·61	29·90
Widowed, Divorced	61	72	6,825	111·89	94·79
Other	3	3	145	—	—
Total	332	402	17,479	52·65	43·48
Females:					
Not known	1	1	4	—	—
Single	69	80	5,385	78·04	67·31
Married	146	186	8,103	55·50	43·56
Widowed, Divorced	170	195	15,521	91·30	79·59
Other	4	4	760	—	—
Total	390	466	29,773	76·34	63·89

the foregoing tables, Fig. 1, and data given elsewhere, that the natural history of this disease differs strikingly between the two sexes. Finally, it is of interest that while in the younger age groups the mean duration of hospital spell tends to be a little longer in men than in women, the opposite is the case after the age of 45 years. When this comparison was made by marital status the biggest difference was found for the married, with a stroke causing a married man to spend an average of 37 days in hospital as compared with an average of 55 days for a married woman. On average, single women stay in hospital for the care of cerebrovascular disease about 10 days longer than single men, but the exact opposite is true for the widowed or divorced.

Discussion

Incidence Data

Attention has already been drawn to the differences in sex-specific incidence rates by age for the haemorrhagic conditions on the one hand and for infarction and the miscellaneous group on the other. If these are expressed as ratios in subarachnoid haemorrhage and cerebral haemorrhage they are 1·0 or less, but in the other conditions they are more than 1·0. The sex differences in subarachnoid haemorrhage are particularly striking, and attention has been drawn to them by others (du Boulay, 1965; Locksley, 1966). The mean age for men in the present study is about 54 years and that for women 60 years, values which differ little between Tables I and V and which bear comparison with 46·8 and 55·5 years reported by Locksley (1966). Though ratios based on the present values are noticeably higher, they show the same tendency for subarachnoid haemorrhage to affect women later in life than men. An analysis not shown here (Acheson and Fairbairn, 1970) indicates that subarachnoid haemorrhage is the most stable of all diagnoses within the categories under investigation, an observation consistent with the work of Florey *et al.* (1967, 1969) on death certificates in New Haven, Connecticut. Since it is unlikely that these differences can be ascribed to the longer stay in hospital in older women with cerebrovascular disease, it must be assumed that they are due to its natural history as this relates to sex.

Cerebral haemorrhage and cerebral infarction are the two largest diagnostic groups. Though there are some small incidence studies of cerebrovascular disease published from the United States—for example, Kannel *et al.* (1965) and Kurland *et al.* (1967)—the only one which is large enough and published in sufficient detail for comparison with the present data is that of Eisenberg *et al.* (1964). These comparisons are shown in Fig. 1. When studying them, some differences in definition should be borne in mind. In the Middlesex study "no differentiation was made between subarachnoid haemorrhage and intracerebral haemorrhage"; thus it is not possible to compare the incidence of subarachnoid haemorrhage in the Oxford area with Middlesex data (Fig. 1 A), and the difference between the curves for Middlesex and Oxford in Fig. 1 B are in part due to the fact that the former includes both types of haemorrhage. If, however, the combined rates for the two kinds of haemorrhage in Oxford are added, they are slightly in excess of those for Middlesex. The curves shown in Fig. 1 C are not strictly comparable either, because the Oxford data combine cerebral thrombosis and embolism, but four cases of cerebral embolism were excluded by Eisenberg and his colleages from the Middlesex curve. The inclusion of these cases would, however, make the differences between the two curves even greater, so that it is evident that the reported incidence of infarction in Middlesex is consistently higher than in Oxford.

In general, strokes of undetermined type tended to be a little more frequent in Middlesex than in Oxford (Fig. 1 D). Not too much should be made of these individual differences, partly because of the different methods of classification in the two studies, and partly because the basis for medical diagnosis is unlikely to be identical in the two areas—a point to which we shall return. The comparisons made in Fig. 1 E, however, where the categories are pooled, are probably less affected by differing standards of medical and statistical classification. These pooled data show a remarkable similarity for the incidence rates for women in the two communities up to the age group 65-74 years, after which the Middlesex rates increase more rapidly than the Oxford rates. In males, however, the Middlesex rates tend to be higher throughout. If, as we have suggested above, our assumptions lead to underestimates of the incidence in Oxford, the two sets of data may be even more similar than they appear to be.

Survival

Attention has already been drawn to the close comparability of survival rates in the Oxford and Middlesex studies when all the cases are considered together. If, however, the categories are taken separately there are again very definite discrepancies between the two studies. Reported survival rates from cerebral haemorrhage are much longer in Oxford than in Middlesex, and would continue to be so even if the cases of subarachnoid haemorrhage were included among the former data; in contrast the survival from cerebral infarction is less in the English than in the American study. These differences most likely stem from differences in diagnostic fashion; for instance, if death within 48 hours of an apoplectic seizure were taken as an important criterion in the diagnosis of cerebral haemorrhage in Connecticut but not in Oxfordshire, this of itself could account for the difference.

Our estimates of hospital-based survival data (not shown) were more similar to the studies which report on the survival of all stroke admissions to hospital (Carroll, 1962; Howard *et al.*, 1963; Boyle and Reid, 1965; Conant, *et al.*, 1965) than to several others which are concerned with patients who have survived the initial episode and are the subjects of special studies of therapy or rehabilitation (Pincock, 1957; Lindgren, 1958; Marshall and Shaw, 1959; Robinson *et al.*, 1959; David and Heyman, 1960; Carter, 1964; Katz *et al.*, 1966). As like ours as any are those of Carroll (1962), who reports on 98 men and women with an average age of 67 years admitted to the City Hospitals in Baltimore, Maryland. Their survival rates were: one month 63%, six months 52%, and one year 49%, giving a slightly higher immediate loss rate than in Oxford, but an identical value for one year.

It is worth noting that though the mortality curves in Fig. 1 are concerned with all deaths in the Oxford area in 1963, and the survival data in Table IV are concerned with cases incident in 1963, some of which were terminated by death in 1964, the general patterns in the figures and the tables are closely similar.

Bed Usage

In general the information shown in Table V bears out for individual people the data published by the Hospital Inpatient Enquiry for hospital spells (Ministry of Health and General Register Office 1967, 1968). A few of the findings are, however, of sufficient importance to merit mention. The fact, alluded to above, that after the age of 45 a woman with cerebrovascular disease makes much heavier demands on the hospital service than a man of the same age, and that the difference lies almost entirely among those at present married, would indicate that this is a social phenomenon. Apart from the few cases of subarachnoid haemorrhage already discussed, there is no other indication in the data that the natural history of cerebrovascular disease differs enough between men and women in this age group to account for their different service demands. It seems that a married middle-aged or elderly man is less well able to cope with a semi-paralysed spouse than a woman in this age group, so that a stricken wife must stay in hospital but a husband can go home. This problem might lend itself to a more economical and acceptable solution than the prolonged occupation of a general hospital bed—and here it is pertinent to point out that in 1964 fewer beds per unit population in the Oxford Region* were assigned to women with cerebrovascular disease than in any other region in England and Wales, and in 1963 only the Liverpool and Wessex Regions were lower in this respect (Ministry of Health and General Register Office, 1967, 1968).

Finally, the data presented here show very clearly that attempts to judge from mortality data the magnitude of the problem posed by cerebrovascular disease in persons aged less than 65 years lead to considerable underestimates. If hospital admissions are taken into account it is estimated that about 27% of all incident cases occur in persons of working age. As judged by the extent of bed usage or survival among these younger sufferers, their morbidity lays a substantial burden on society. Quite apart from their need for prolonged medical care, their loss of working capacity is considerable. The Hospital Inpatient Enquiry shows that between 40 and 50% of all spells in hospital for treatment of cerebrovascular disease last more than a month, and this proportion is almost wholly independent of age. The higher average duration of stay in the oldest group is due to a small proportion (less than 8% in 1963) whose spell in hospital lasted more than eight months.

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*Much larger than the Oxford Record Linkage Study area, but wholly inclusive of it.

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Serum Gastrin in Patients with Peptic Ulceration

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Summary: The fasting serum level of gastrin was determined by radioimmunoassay in 41 normal subjects, 27 patients with duodenal ulceration, 12 patients with gastric ulceration, and 8 patients following "complete" vagotomy. The patients with duodenal ulceration had significantly higher serum levels of gastrin (1·3 ± S.D. 0·7 ng./ml.) than normal subjects (0·4 ± S.D. 0·3 ng./ml.), patients with gastric ulceration (0·4 ± S.D. 0·4 ng./ml.), or post-vagotomy patients (0·15 ± S.D. 0·2 ng./ml.).

The gastrin secretion in both normal subjects and patients with duodenal ulceration was responsive to protein ingestion, but a larger incremental secretion of gastrin occurred in the latter group. Hyperglycaemia significantly suppressed the serum level of gastrin in both groups. The patients with gastric ulceration had fasting and postprandial serum gastrin levels not significantly different from normal subjects.

Introduction

Gastrin was the second hormone discovered (Edkins, 1905), but until recently no disease state had been associated with abnormalities in its secretion. It is now known that the Zollinger–Ellison syndrome (Zollinger and Ellison, 1955) is caused by pancreatic tumours secreting abnormal amounts of gastrin (Gregory *et al.*, 1967; McGuigan and Trudeau, 1968; Odell *et al.*, 1968), thus causing the high basal acid secretion and intractable peptic ulceration characteristic of this disease. Patients with duodenal ulceration also have an excessive basal secretion of acid (Levin *et al.*, 1948; Woodward *et al.*, 1949), and the demonstration (by bioassay) of increased amounts of gastrin in their antral tissues (Emås and Fyrö, 1964) indicates that an abnormality in gastrin secretion may also be important in the pathogenesis of this disease. In this study a sensitive radioimmunoassay has been used to determine the levels of gastrin in the sera of normal subjects and patients with peptic ulceration.

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Patients and Methods

All investigations were conducted with the patients in bed in a quiet room after an overnight fast. Anticholinergics were suspended 18 hours before examination. Venous blood samples were obtained from a plastic catheter inserted into an antecubital vein 20 minutes before starting the study. The blood was allowed to clot at 4°C., then centrifuged, and the serum separated and stored at −10° C. until assayed. The normal subjects consisted of medical and paramedical personnel. Informed consent was obtained before beginning the study. The subjects had no personal or family history of gastrointestinal disease.

The peptic ulceration groups consisted of patients with duodenal or gastric ulceration who had been admitted to the inpatient or outpatient section of this hospital. Patients with duodenal ulceration had radiological evidence of a duodenal crater ± scarring, while the patients with gastric ulceration had radiological ± gastroscopic evidence of a benign gastric ulcer. Prepyloric or combined gastric and duodenal ulcers were excluded from this study. All the patients had "active" disease—that is, they had suffered a complication or had definite symptoms from their ulcer within the previous two weeks.

The post-vagotomy group had undergone bilateral truncal vagal section for duodenal ulceration six weeks to five years before examination. The gastric acid response to insulin-induced hypoglycaemia was used to assess the completeness of vagotomy according to the criteria of Hollander (1948).

Fasting Levels.—Fasting venous samples were obtained