Fifty instances of leukaemia in association with mongolism are known to have occurred in England and Wales between 1945 and 1959. The proportion of deaths attributed to the various types of leukaemia are closely similar to those estimated from the national mortality rates, and it is concluded that the increased risk of acute leukaemia in mongolism affects all the types of the disease commonly observed in childhood.

Examination of the death entries relating to 5,425 children who had died of leukaemia or aplastic anaemia revealed only one example of the occurrence of one or other disease in both members of a pair of identical twins.

We are grateful to the Registrar-General of England and Wales for the extraction of the data; to Professor M. Segi for details of the leukaemia mortality in childhood in Japan; to Dr. Alice Stewart for details of some of the cases of associated mongolism and leukaemia; to Dr. R. A. M. Case for information about the mortality rates for leukaemia in childhood in England and Wales between 1911 and 1930; and to Dr. A. G. Gilliam for information about population estimates in the U.S.A. We are grateful also to Dr. Jean Kennedy, Mrs. V. Peetz, and Mrs. J. Pixner for assistance in the analysis.

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"The late Dr. Robert Scot Skirving, a self-styled 'remembrancer' of Australian medicine, spoke of Joseph Bancroft [1836–94] with reverence and admiration. 'There seemed to be nothing in the friendly, untidy town that was Brisbane,' he said, 'that Bancroft was not connected with in some way or other. He knew a lot, and always made it his job to be helpful. He was consulted by everyone in the place, from the Government down. He was just the man for a new country.' The final observation of this wise and critical physician is especially revealing of the characters that brought esteem to Bancroft in his day, and raised the Bancroft tradition. He was just the man for a new country—this is the sum of all his qualities. It includes his deep knowledge and searching mind, his resourcefulness, his self-reliance, and his untiring industry; it includes the extreme utilitarianism that was his hall-mark, and his widely diversified interests; and it surely includes his dedication to his profession and his scientific aims, his full acceptance of community responsibilities and his leadership in all fields of interest. These are the foundations of the Bancroft tradition—the tradition of a great colonial doctor." (Professor Edward Ford, Bancroft Memorial Lecture, *Med. J. Aust.*, February 4, 1961.)

ACUTE MYELOID LEUKAEMIA IN ADOLESCENTS

BY

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The death-rate from leukaemia is high in young children, and then falls to a minimum in early adult life. In the course of studies on morbidity and mortality in adolescents (Lee, 1961) it was noticed that in males the decline in the leukaemia death-rate during adolescence was interrupted by a transient rise (Fig. 1). This excess mortality is not a new phenomenon, but goes back at least to 1911–15. A study of this phenomenon is now reported.

FIG. 1.—Death-rates from leukaemia in males and females by age. England and Wales, 1950–58 (General Register Office, 1957; 1958).

Method

The General Register Office for England and Wales, the General Registry Office for Scotland, the United States National Office of Vital Statistics, and the Canadian Dominion Bureau of Statistics were asked to provide the number of deaths certified to leukaemia by single years of age, over the range 0–29, for as many calendar years as possible. Figures for 1945–57 in England and Wales, for 1950–58 in Scotland, 1950–57 in the United States, and 1949–58 in Canada, were obtained, together with the corresponding population estimates, through the courtesy of these offices.

Leukaemia is not a common disease, and to obtain adequate numbers the data for the whole of the periods available have been combined. In the analysis of mortality, two-year age-groups were found to be a suitable compromise between single years of age, which resulted in too great variations due to small numbers, and conventional five-year age-groups, with their possible obscuring of changes limited to short periods of life.

Further data were provided for 1949–57 through the courtesy of the National Cancer Registration Scheme for England and Wales. A substantial and growing proportion of the cases of malignant disease are reported to this registration scheme, but during these years the number of cases of leukaemia reported in persons aged 15–19 was only about 40% of the deaths certified to leukaemia in England and Wales. Thus division by five-year age groups was the smallest that could usefully be made of these data. Much more information was available about these cases than can be derived from the

analysis of death certificates—for example, on the duration of the illness.

Results

Analyses of the mortality data are shown for England and Wales, for Scotland, for the United States, and for Canada in Fig 2. In each of these four countries the decline of the death-rate with age stops at about 13 in males, and then rises to a new peak at about 17. A

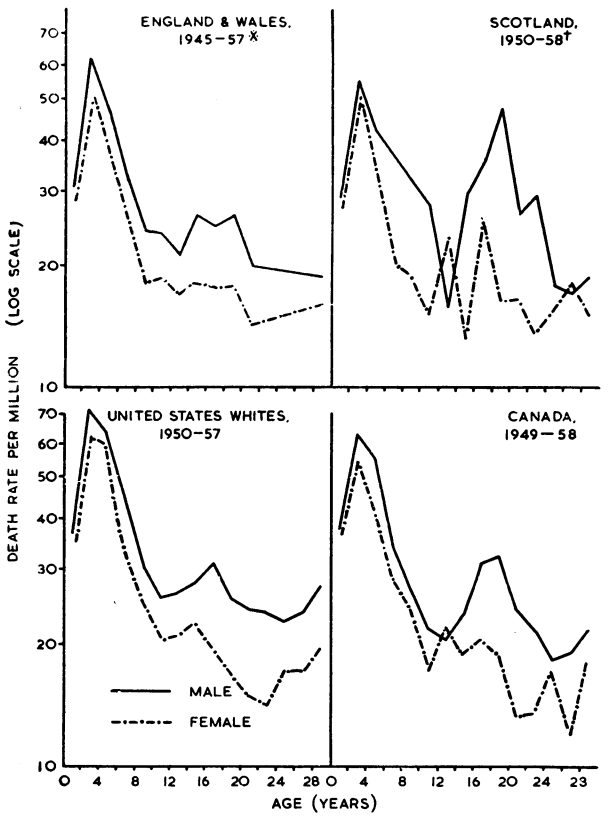

FIG. 2.—Death-rates from leukaemia in males and females by age. (*5-year age-groups 20–24 and 25–29, due to lack of official population estimates. †Based on small numbers).

further decline then occurs, and continues until the late twenties. In females there is evidence of a similar trend, but it is less marked. In the United States and Canada the rise in females appears to occur earlier than in males.

The data from the National Cancer Registration Scheme show a small increase in all leukaemia in males aged 15–19, compared with neighbouring age-groups (Table I). This rise is restricted to cases described by the physician as "acute." Further, these extra cases in male adolescents are concentrated among the acute leukaemia cases with histories of less than two months between the reported onset of symptoms and admission

TABLE I.—*Number of Cases of Leukaemia Notified to the National Cancer Registration Scheme, 1949–57*

Age:	<5	5–	10–	15–	20–	25–	30–	35–	40–	45–49
Male										
Acute ..	178	116	78	87	69	49	44	63	75	80
Other and unspecified	66	54	44	47	56	96	100	121	184	246
Total ..	244	170	122	134	125	145	144	184	259	326
Female										
Acute ..	132	83	59	43	34	39	41	44	39	49
Other and unspecified	56	48	26	38	42	63	70	112	146	213
Total ..	188	131	85	81	76	102	111	156	185	262

TABLE II.—*Number of Cases of Leukaemia Specified as Acute with Histories of Less than Two Months and Number with Longer or Unspecified Histories. National Cancer Registration Scheme, 1949–57*

Age:	<5	5–	10–	15–	20–	25–	30–	35–	40–	45–49
Male										
Acute with history of under 2 months ..	90	51	37	52	29	18	**16**	25	33	27
Acute with history of other and unspecified duration ..	88	65	41	35	40	31	28	38	42	53
Female										
Acute with history of under 2 months ..	73	41	23	19	13	15	13	12	14	15
Acute with history of other and unspecified duration ..	59	42	36	24	21	24	28	32	25	34

TABLE III.—*Number of Cases of Leukaemia Specified as Acute, by Length of History and Cell Type. National Cancer Registration Scheme, 1949–57*

Age:	<5	5–	10–	15–	20–	25–	30–	35–	40–	45–49
Male										
History of under 2 months:										
Myeloid ..	17	9	10	27	14	2	12	12	15	16
Lymphatic	32	23	18	10	8	9	2	6	8	6
Other and unspecified	41	19	9	15	7	7	2	7	10	5
History of other or unspecified duration:										
Myeloid ..	17	11	11	13	16	15	14	21	24	28
Lymphatic	29	23	19	11	12	4	6	7	4	8
Other and unspecified	42	31	11	11	12	12	8	10	14	17
Female										
History of under 2 months:										
Myeloid ..	10	11	5	10	5	4	9	7	8	5
Lymphatic	32	14	6	6	3	2	2	3	0	2
Other and unspecified	31	16	12	3	5	9	2	2	6	8
History of other or unspecified duration:										
Myeloid ..	11	9	10	8	10	14	16	20	11	21
Lymphatic	22	18	11	4	6	6	6	4	5	5
Other and unspecified	26	15	15	12	5	4	6	8	9	8

to hospital (Table II).* Analysis of these cases of acute leukaemia with particularly short histories by cell type shows that the excess at age 15–19 is not found in the lymphatic type, but only in those of myeloid type (Table III, Fig. 3). Moreover, those of myeloid type with a longer history do not show the effect either. The age distribution of these cases of acute myeloid leukaemia with short histories is quite different from that of the rest of leukaemia.†

*The length of survival after diagnosis of the cases notified to the National Cancer Registration Scheme was also recorded, but the method of tabulation was changed in the middle of the period of observation. There are not enough cases in either of the series thus produced for an analysis to be made of survival by five-year age-groups. However, an analysis by ten-year age-groups suggests that short histories before admission do go with short survival.

†Comparing acute myeloid leukaemia with a short history with the rest of leukaemia, using the male data of Tables I–III, $\chi^2 = 48.6$, 9 d.f. $P<0.001$. The contribution to the total χ^2 of the age-group 15–19 alone is 33.3. Only two cases of acute myeloid leukaemia with a short history were notified in males aged 25–29; as the result this age-group makes a contribution of 7.4 to the total χ^2. The small number of cases in this age-group is an isolated finding which requires confirmation before its interpretation can be attempted.

Because the National Cancer Registration Scheme did not include all cases, and the cases included might have been unrepresentative, it was necessary to check the indication that it is myeloid and not lymphatic leukaemia that is responsible for the rise in adolescents. The published national mortality data for leukaemia are divided by cell type but are not divided into the acute and chronic forms of the disease. However, for ages from 15 a special analysis including this division has been made by Court Brown and Doll (1959). In addition, I have assumed that from 0–14 the published deaths were all due to acute leukaemia, chronic leukaemia in this age-range being uncommon (cf. MacMahon and Clark, 1956; Witts, 1956). The death-rates from acute lymphatic leukaemia show a fairly steady decline from childhood to at least the age of 30 (Fig. 4). In contrast, the rates for acute myeloid leukaemia show a rise in males aged 15–19 (Fig. 4).

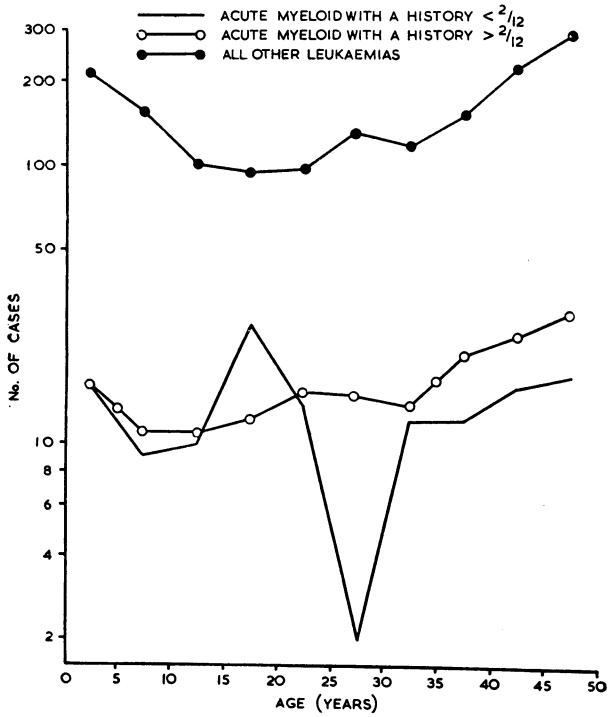

FIG. 3.—Number of male cases of leukaemia reported to the National Cancer Registration Scheme, 1950–57, by age.

Thus in England and Wales, Scotland, the United States, and Canada, males in their teens have an increased mortality from leukaemia compared with neighbouring age-groups. This effect is wholly or almost wholly accounted for by an increased incidence of a form of acute myeloid leukaemia which runs an especially short course before admission to hospital. Chronic leukaemia and acute myeloid leukaemia with a history of more than two months do not appear to contribute to this increase.

The same phenomenon is found in females but is less conspicuous, and it may occur at an earlier age.‡

Discussion

The data from England and Wales suggest that the death-rate from leukaemia in males aged 15–19 is about 6 per million per annum greater than would be expected if the trend of the rates with age was not interrupted in this period (Fig. 2). The male population of this country in this age-group is 1.4 million, so that the whole effect described in this paper is due to about 10 cases occurring annually. This figure gives a measure of the difficulty of studying the problem. However, the smallness of the numbers is due to the rarity of leukaemia of any sort rather than to the smallness of the increase in adolescents. Inspection of Fig. 2 suggests that the death-rate in males is increased by about 25% during this period.

Relatively high death-rates at ages 15–19 from leukaemia in males have been present in England and Wales since at least the early 1910's. The peak has not moved along the age scale, and

‡The excess myeloid leukaemia in adolescents is most obvious in males, and it would be expected that the sex ratio of all leukaemia at this age would be altered by these cases. This may happen, but the effect is lost in a large rise in the ratio of male to female cases of leukaemia which occurs at this age, and which is not restricted to the myeloid cell type. This has a wider age-range than these special cases of acute myeloid leukaemia with a short history, and seems to be part of a quite different phenomenon. A study of these changes is in progress.

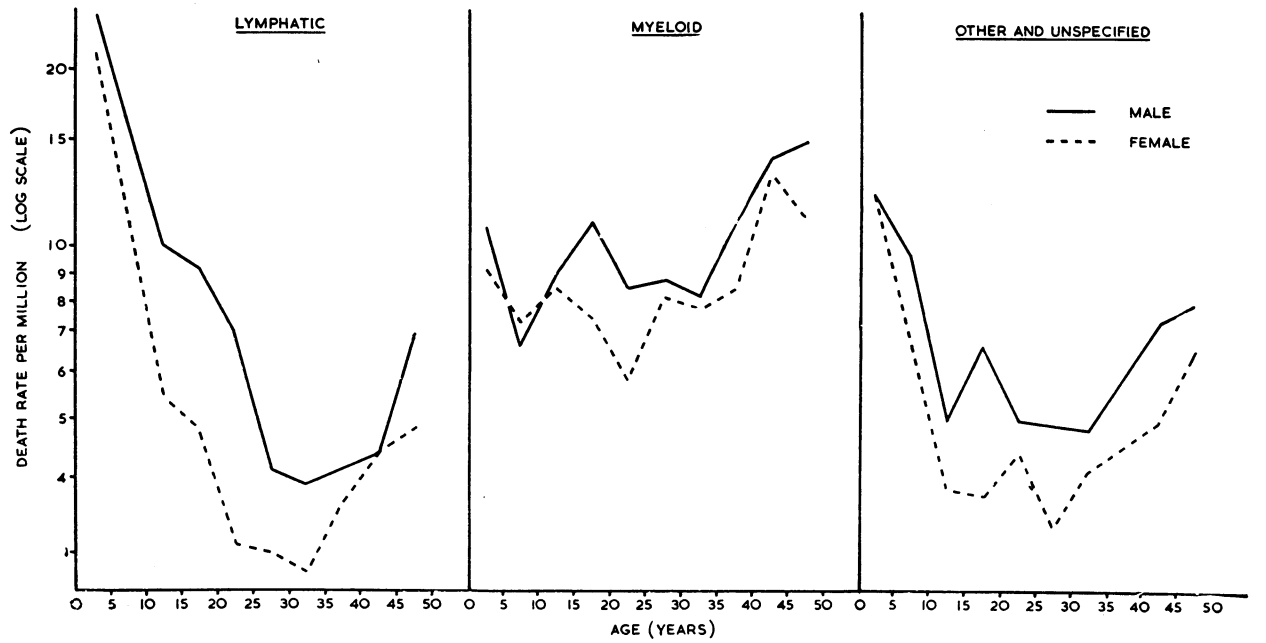

FIG. 4.—Death-rates from acute leukaemia in males and females by age, England and Wales, 1950–57.

thus a "cohort effect" is not present. Since that period, death-rates from leukaemia have risen at all ages, but they have risen at least as much at 10–14 and 20–24 as at 15–19. The peak in adolescents is therefore unlikely to be due to the same causes that have produced the rise in the death-rate from leukaemia at all ages in recent decades. There is no evidence on which to base any discussion of the relationship of these cases of leukaemia to radiation.

The high leukaemia rates in male adolescents are matched by corresponding increases in admissions to hospital for acute infections of the lower respiratory tract (Fig. 5). In females the rise in the number of hospital admissions for these conditions is similar, but, as already pointed out, in England and Wales at least

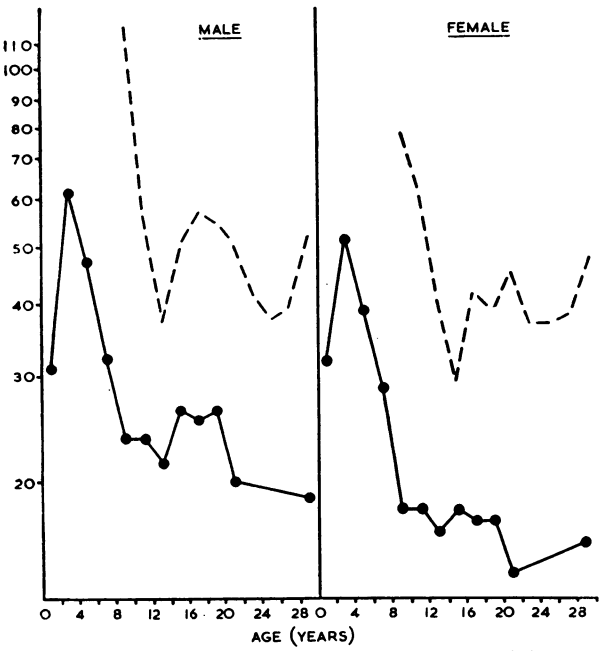

FIG. 5.—Leukaemia and acute lower respiratory infections. ----, Hospital admissions for bronchitis and pneumonia: National Hospital In-patient Inquiry, England and Wales, 1953–56. ●——●, Leukaemia death rates, England and Wales, 1945–57.

the change in the female leukaemia rate is less marked. These are interesting findings, because in children under the age of 10, Stewart (1961) has put forward evidence that pneumonia may induce leukaemia after a short latent period. There is very little other evidence on the possible causation of a special form of leukaemia in adolescents; but it is perhaps worth mentioning that myeloid leukaemia is a disease of bone-marrow, and that the incidence of malignant disease of bone is much higher in adolescents than in children or young adults (Fig. 6). Adolescence is a period of rapid bone-growth (cf. Tanner, 1955; Furth, 1959), and a period when lymphoid tissue regresses—and there is no increase in lymphatic leukaemia. The known causes of leukaemia are few in number, and only a small proportion of cases can be associated with them (*B.M.J.*, 1960; Gunz, 1961). There is a factor which affects adolescents specifically, and which produces a substantial increase in the death-rate from a particular form of leukaemia. There is no reason to associate this with any of the known causes of leukaemia.

The identification of a syndrome by the study of the characteristics of cases in relation to the population from which they come is a typical and successful use of modern epidemiology (Morris, 1957). Further, with a rare disease such as leukaemia the accumulation of data by such means as cancer registries is essential. Both these techniques have been exploited in this study, and it is difficult to see how these special cases of myeloid leukaemia could have been found without them. But studies such as these are dependent on mortality and morbidity data being routinely compiled and made available in sufficient detail for the necessary analyses to be made.

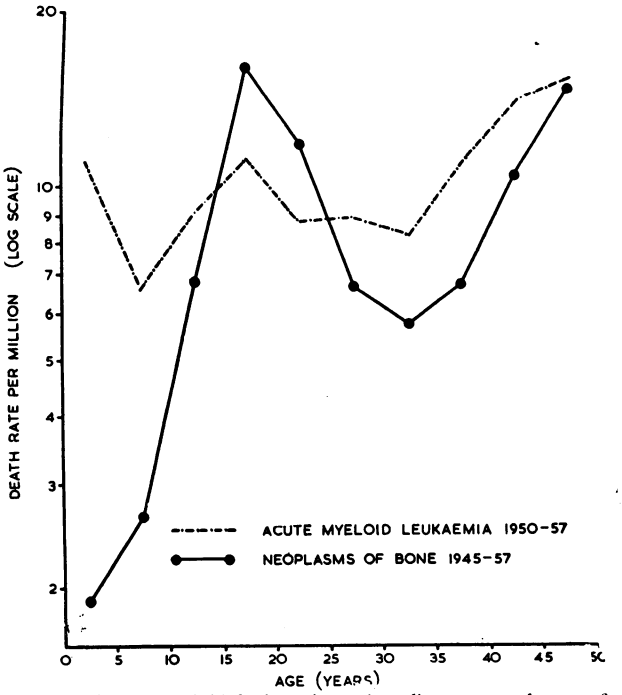

FIG. 6.—Acute myeloid leukaemia and malignant neoplasms of bone in males by age, England and Wales.

Summary

The death-rate from leukaemia in males in their late teens is higher than expected in England and Wales, in Scotland, in the United States, and in Canada. In England and Wales in the years 1945–57 the male death-rate per million per annum was as follows:

Death Rate from Leukaemia in Males (Ages in Years)

6–	8–	10–	12–	14–	16–	18–	20–24	25–29	30–34	35–39	40–44
32·0	24·2	24·0	21·5	26·1	25·0	26·4	20·1	18·5	21·7	25·9	31·3

The effect in females was less marked.

In the National Cancer Registration Scheme for England and Wales the number of male cases diagnosed as acute myeloid leukaemia which had histories before admission of less than two months rose from 10 at ages 10–14 to 27 at ages 15–19 and then fell to 14 at ages 20–24. No similar excess was found in cases with longer histories or other cell types.

The death-rate from leukaemia thus is raised in late adolescence, particularly in males; and this seems to be due to an increased incidence of a form of acute myeloid leukaemia with a short history before admission to hospital.

I am grateful to the General Register Office of England and Wales, to the General Registry Office of Scotland, to the Chief of the United States National Office of Vital Statistics, and to the Canadian Dominion Statistician, for the tabulations of mortality and the population tables that

went with them. The Medical Records Officers of the London Hospital and St. Bartholomew's Hospital kindly supplied data about their cases of leukaemia. The late Dr. A. Mackenzie, of the General Register Office, suggested the analysis of the cases by length of history and was most helpful in other ways. Dr. Richard Doll kindly made analyses of mortality data available. Professor J. N. Morris and my colleagues in the Social Medicine Research Unit and the London Hospital gave me much help.

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ACCIDENT NEUROSIS*

BY

HENRY MILLER, M.D., F.R.C.P., D.P.M.

LECTURE II

The preceding lecture comprised an account of the incidence, clinical features, and natural history of accident neurosis, based on the records of personal cases. The syndrome is seen to present a unique combination of clinical features, amongst the most remarkable of which are an inverse relation to the severity of the provoking injury; an unexpectedly inconstant correlation with neurotic predisposition; scanty objective signs of emotional disturbance; a differential social incidence; and an absolute failure to respond to therapy until the compensation issue was settled, after which nearly all the cases described recovered completely without treatment. These are observed facts, but a consideration of the nature of the syndrome raises more difficult matters of interpretation and speculation.

In subjecting this material to critical scrutiny the first question may well be, how far is there such a thing as accident neurosis? Is this anything more than a convenient label of the kind often employed to spare the investigator further thought about a difficult clinical problem—in this instance the behaviour of a heterogeneous minority of people injured or otherwise involved in accidents? It was with considerable scepticism on this score that I began the present study several years ago. The reader must judge how far the evidence already presented supports my conclusion that, after patients suffering from other definable psychiatric disorders have been excluded, the behaviour of a minority of those involved in accidents is sufficiently characteristic and predictable to justify the acceptance of accident neurosis as a clinical entity. The condition probably affects between a quarter and a third of the victims of accidents which fulfil two conditions. First, the accident must be due to someone else's fault, at any rate in the patient's estimation. Secondly, it must have occurred in circumstances where the payment of financial compensation is potentially involved.

Cursory mention is made in the psychiatric literature of cases in which the syndrome is said to have followed accidents which satisfied the first but not the second of these criteria. Depressive illnesses of endogenous pattern may certainly follow accidents innocent of any financial implications, and very occasionally frank neuroses of anxiety type have been similarly encountered after frightening accidents to predisposed patients, limited in duration and responsive to therapy. It is possible that the florid syndrome of accident neurosis outlined above, with its disproportionate disability and absolute resistiveness to treatment, occasionally occurs after accidents occurring under emotionally loaded circumstances in which no question of financial compensation is concerned, but such cases have not been personally encountered.

Whatever the cause of accident neurosis, it is not the result of physical injury. It may develop without any injury at all, it is comparatively uncommon where injury has been severe, and it is characteristically a complication of minor or trivial injury. Indeed, the inverse relationship to the severity of injury clearly evident in the material described above is crucial to its understanding, and makes nonsense of some "explanations" of the condition.

It is difficult to believe, for example, that any form of constitutional difference between those severely and those trivially injured can account for the apparently "protective" effect of severe trauma against the development of neurosis in these patients, most of whose injuries are sustained in similar industrial circumstances, equally subject to whatever emotional loading is implicit in the employee–employer relationship in such situations. Another interpretation is that the genuinely injured patient, reasonably confident of justice in the matter of compensation, does not need a neurosis, while the grazed or frightened workman develops neurotic symptoms which inflate his trivial or non-existent physical disability to dimensions justifying financial compensation.

But why do only a third of those involved in minor accidents succumb to accident neurosis? The only factual evidence is that such a development is favoured by a low social and occupational status, and that its relationship to a history of psychoneurotic predisposition is surprisingly inconstant—a feature which distinguishes it from almost every other disabling neurosis beginning during adult life, and one which must be regarded as highly significant in any consideration of the nature of the syndrome.

The occurrence of accident neurosis in predisposed subjects is anything but surprising, and the role of predisposition in the persistence of disability after settlement has been demonstrated in the figures already given: of the five patients in whom the condition persisted, four were grossly predisposed to neurosis. However, many patients with accident neurosis have carried on their work for many years before the accident without any trace of psychiatric disability and with little loss of time. Indeed, this feature is often quoted in court to support the genuineness of the patient's complaints. Why do a minority of such patients develop this disabling syndrome? An orthodox psychiatric explanation is that the trivial injury, or the concatenation of circumstances surrounding it, implies devastating

*From the Milroy Lectures for 1961, delivered before the Royal College of Physicians of London on February 7 and 9. Lecture I appeared in last week's issue.