and mitigate the severity of those which do occur, by by-passing the morphological issue and, as an expedient, raising to prophylactic levels the amount of anticoagulant substance derived from humoral sources normally circulating in the blood. At the present time this is possible experimentally: when introduced into the portal circulation, curare increases the output of heparin from the liver. Unfortunately, even if a suitable pharmacological preparation were available, therapy of this kind would need to be continuous, for we do not know whether a tendency to clotting—"pre-clotting"—precedes episodes of thrombosis by a long period or a short one. Moreover, investigation along such lines might not commend itself, because on occasion clotting is a valuable protective mechanism, and to suggest its abolition transgresses a clinical precept which is usually sound enough—that one must never try to correct one pathological process by substituting another; although in this particular problem I should not subscribe to that view.

Conclusion

I fear that, by selecting so vast a subject as ischaemia to be the topic of this Memorial Lecture, I have been constrained to be so eclectic that it may seem to lack continuity. If that be so, the fault is mine.

While I was engaged in preparing the address, more than once I had the feeling that here was a matter on which I should have liked to enlist Horsley's advice and help. I venture to repeat that the lecture has been designed to illustrate that oneness of the laboratory, the ward, and the operating theatre so well exemplified by Horsley's life's work. Indeed, there is something more than oneness. For there is holism in surgery as well as in philosophy—the tendency for the final accomplishment to be greater than the sum of the contributions from each of these three arbitrary divisions of our efforts.

To few in our profession have been given those twin gifts without price: the genius to produce ideas, and the steadfastness of purpose to pursue their ideas as ideals. Such a one was Victor Horsley.

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Two new American journals were published in January, —*Applied Microbiology* and the *Journal of Histochemistry and Cytochemistry*. The agents in this country are Messrs. Baillière, Tindall and Cox, and orders for the journals may be sent direct to them or placed with any bookseller. Annual subscription for *Applied Microbiology* is 63s. post free, and the journal will be published bi-monthly. The other journal is the official organ of the Histochemical Society of America, costs 60s. per annum, and will also appear bi-monthly. The *American Surgeon* is the new name given to the *Southern Surgeon*, official publication of the South-eastern Surgical Congress of America, to mark its widened scope as a general surgical journal. It is published monthly, annual subscription 82s. Messrs. Baillière, Tindall and Cox are the British agents.

HEALTH OF PREMATURE CHILDREN FROM BIRTH TO FOUR YEARS*

BY

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AND

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This paper describes the health of a national sample of premature children who have been observed during the first four years of their lives and compared with a carefully chosen group of "controls." Details of their growth and development will be published in subsequent papers.

Some 40,000 of the babies born each year in Great Britain weigh at birth 5½ lb. (2.5 kg.) or less, and by international agreement are classed for statistical purposes as premature. Approximately a quarter of them die before they are a month old, and it has been claimed that many of the survivors, as a consequence of prematurity itself or of the antenatal conditions leading to it, are sickly, stunted, or mentally retarded. It is probable that in the future we will be able to save the lives of more of these babies, and it is important to know how large a proportion will be handicapped in later life and what institutional or other special care they will need.

At first sight it seems that these questions could be easily and directly answered by tracing in later life children who had been prematurely born. Many studies of this type have in fact been made, the majority being concerned with growth and development rather than with health. But the results have been conflicting. Some reveal prematurity as a major cause of mental backwardness and dwarfed growth, whereas others show premature children as retarded only to the extent that they were born before term.

The difficulties of tracing children after a lapse of years are great, and few investigators have found more than half the survivors for whom they were looking. Moreover, depending on the channels through which they have had to work, some appear to have been more successful in tracing the abnormal children and others in tracing the normal ones. They have also, in general, been content to compare the health and development of premature children with "national averages," often obtained many years earlier from highly selected groups and by methods differing widely from those used in their own inquiries. A few have compared premature children with a random sample of children born at term during the period of their inquiry, and others have compared each premature child with its sibs. None of these methods is satisfactory, because prematurity is not distributed at random in a series of births. Premature children tend to be female, to be first-born, to come from the poorer classes, and to have mothers who are above the average age for child-bearing. And unless they are

*This follow-up survey of premature children is being made by a joint committee of the Institute of Child Health (University of London), the Society of Medical Officers of Health, and the Population Investigation Committee. The chairman of the Committee is Professor James Young, the vice-chairman Professor A. A. Moncrieff, and the secretary Professor D. V. Glass. The Nuffield Foundation has financed this inquiry during the pre-school years, and a grant for continuing it in the primary school period has been made by the Board of the Hospital for Sick Children, Great Ormond Street, through the Institute of Child Health.

compared with mature children chosen to conform to this pattern it is doubtful what weight can be attached to any differences in growth or health that are observed. It is likely, then, that the conflicting results of previous studies have arisen from the difficulties of obtaining an adequate sample of prematurely born children and of finding a suitable group of children born at term to compare them with.

Description of the Present Survey

We have had the good fortune to follow up over a period of four years the health and development of a national sample of children who weighed at birth 5½ lb. (2.5 kg.) or less and to compare them with a carefully selected group of children who were heavier at birth.

This sample was obtained in 1946, when a Joint Committee of the Royal College of Obstetricians and Gynaecologists and the Population Investigation Committee, with the help of medical officers of health and health visitors throughout the country, investigated all confinements taking place in England, Wales, and Scotland during the first week in March of that year. Out of a total of 458 maternity and child welfare authorities, 424 took part in this inquiry, and detailed medical and social information was obtained about 91% of the births notified in these authorities during the chosen week. In all, 13,687 women were interviewed by health visitors eight weeks after the birth of their babies. The information given by them and obtained from their records formed the basis of a report on the maternity services (Royal College of Obstetricians and Gynaecologists, 1948).

We have chosen as our sample of premature children all legitimate singletons who were notified to us during the survey week and who weighed 5½ lb. or less at birth. We are, of course, aware that not all babies of this weight are premature in the sense that they are born before term. But the weight standard of prematurity is generally accepted, and has been used in the more recent studies of the health, growth, and development of premature children; and it would be foolish to present our material in a form that could not be compared with the results of many of the studies that had preceded it. To talk about "children weighing 5½ lb. or less at birth" is clumsy, and we have preferred to use the term "premature" to describe them, since, although inaccurate, it is established by long usage. For the same reason we have not attempted to use different weight standards of prematurity for the two sexes.

Each premature child in the sample was paired with another child selected from the remaining legitimate single-born children in the sample, who was of the same sex, age, and place in the family, who came from the same type of home background, lived in the same locality, and had parents of the same age and social class. We have been able to match the majority of the pairs very closely owing to the large numbers of children from whom we could draw; even so, a perfect match was not always forthcoming, and a certain latitude has been allowed. For example, if a suitable match for a premature child could not be found within the area of the authority where he was born, the search was extended to other similar authorities in the same geographical region; 17% of the pairs were matched from different authorities. It was also not always possible to match exactly for birth order. While first births were always paired with first, second births might be paired with third, and third births with second or fourth, etc. During the course of the inquiry a few mistakes in matching were found, and then the original control was discarded and a new one chosen. A premature child was also re-matched when his paired control had left the country; but when either member of a pair had died the survivor was retained in the survey.

Health visitors saw these children and interviewed their mothers on three occasions—when they were 2 months, 2 years, and 4¼ years old. At these interviews information was obtained on home conditions, hospital admissions, colds, and certain specified illnesses, and arrangements were made to weigh and measure the children at welfare centres. Information about the course and duration of pregnancy and the care given to the child after birth was obtained from the records of hospitals and midwives.

This comparative study of children born prematurely and at term is part of a much larger inquiry into the health, growth, and development of a national sample of children. This larger inquiry (which will be referred to as the "main survey") is mentioned here because it provides figures on deaths and illnesses which are referred to in this paper. The detailed planning of it has been described elsewhere (Douglas, 1951).

Loss from the Sample

Birth weights of 5½ lb. or less were recorded for 851 single-born children in the 1946 sample, of whom 67 were stillborn and 72 were illegitimate, and accordingly excluded from further study. Five of the remaining 712 children were later found to have weighed more than 5½ lb. at birth, and a further 31 were excluded because so little was known of their home backgrounds that they could not be satisfactorily paired with controls. In retrospect we feel it was a mistake to exclude these 31 children, since much of the missing information would have been obtained during the later surveys. We were left with 676 premature children and 676 paired controls, and we have had considerable success in tracing the survivors (Table I).

TABLE I.—*Losses of Premature and Control Pairs, 1946–50*

		No. of Pairs
Unavoidable loss	Death	173
	Emigration (1946–8)	21*
	,, (1948–50)	10*
Avoidable loss	Refusal	6†
	Untraced	2†
Still in survey		464

* Alive at time of emigration.
† All known to be living in 1950.

In this paper our main interest is in the 472 pairs both members of which were still living in this country in June, 1950, when they were 4¼ years old, and the 10 pairs emigrating in 1948–50. Of these 482 pairs, 474 (98.3%) have been successfully retained in the sample, and we have been able to check from official sources that the two children who could not be traced and the six children whose parents refused to help were still living at the time of the last survey. The losses through death and emigration are heavy, but represent a natural decrease in the sample which can hardly be said to have biased it. There is, moreover, no reason to believe that the children who emigrated with their families left this country owing to ill-health; on the contrary, they are likely to be a particularly healthy sample, as all emigrants, including babies, undergo a strict medical examination.

The actual loss of information is rather greater than the figures in Table I suggest. When their mothers were ill or working, the forms for some children were only partly filled in. Other mothers were unable or unwilling to answer certain questions. The loss from these causes varies from table to table, as will be seen below, but for most illnesses it is small.

Survival and Health

(a) Survival

Before describing the illnesses encountered by the 474 pairs of children surviving at 4¼ years, it is appropriate to make a brief comparison of the mortality rates in the premature and control samples. These are shown in Table II, which also gives the equivalent rates for all children in the "main survey sample" who weighed over 5½ lb. This further comparison is required because the mortality rates for the controls, being based on few deaths, are of low precision; but in fact they are similar to and not significantly different from the rates derived from the larger sample.

TABLE II.—*Death Rates of Premature Children, Their Controls, and Mature Children in the "Main Survey"*

Age	Monthly Death Rates per 1,000 Survivors		
	Premature Live Births (676)	Control Live Births (676)	Live-born Mature Singletons in "Main Survey" (5,033)
Neonatal	211·84*	9·11	10·79
1–12 months ..	3·37	1·81	1·09
13 months–4¼ years ..	0·36	0·15	0·19

* Comparing premature children and controls.
For neonatal deaths, $\chi^2=139{\cdot}34$, n=1, P<0·001.
For later deaths, $\chi^2=5{\cdot}27$, n=1, 0·05>P>0·02.

These figures support the view that the high mortality of premature children extends beyond the first month of life. At ages between 1 month and 4¼ years these children appear to be abnormally likely to die from lower respiratory infections, congenital defects, and nephritis, as Table III shows. They are compared, in this table, with the mature children of the main sample and not with their controls, in order to have a greater number of deaths on which to base the comparison. Even so, the numbers are relatively small and the differences in death rates, though statistically significant, need confirmation.

TABLE III.—*Causes of Death Between 1 Month and 4¼ Years*

Causes of Death	Yearly Death Rates per 1,000 Survivors			
	Premature Children (543 Surviving at 1 Month)	"Main Sample" (4,979 Mature Singletons Surviving at 1 Month)	Significance (n=1)	
			χ^2	P
Bronchitis and pneumonia ..	4·88	1·35	10·90	<0·01
Other infections	2·17	1·83	0·002	0·9–0·8
Congenital defects	4·33	0·58	23·00	<0·01
Nephritis ..	1·08	0·05	7·00	<0·01
Other causes ..	1·62	0·63	1·18	0·3–0·2

(b) Nature and Reliability of Our Information on Sickness

Our information on the illnesses of these children was obtained during interviews with their mothers when they were 2 years and 4¼ years old. No comprehensive account of ill-health could be expected to result from this method of approach, and our inquiries were confined to certain specified events and conditions that the mothers would be likely to remember. The following information was asked for and has been used in this paper:

(1) Details of all accidents or illnesses that resulted in admission to a hospital or nursing-home. Mothers were asked to give the reason for admission, the age of the child when admitted, the length of stay, and the name and address of the hospital or nursing-home.

(2) Details of all lower respiratory infections and infectious diseases of childhood which were treated by the family doctor or in an out-patient department of a hospital.

(3) Estimates of the number of colds experienced by each child during the months immediately preceding each interview.

The questionary method is open to several sources of error. Events may be forgotten or they may be so garbled that no useful purpose is served by recording them. They may be remembered but wrongly dated, or they may be attributed, in large families, to the wrong child. We are fortunate in having, for illness resulting in hospital or nursing-home admissions, an absolute check on the extent of these different types of error. During the survey the mothers were asked to give the names of the institutions to which their children were admitted, and we have been able to trace the records of 151 out of the 186 admissions of children in the premature and control sample. Some hospitals had destroyed their records, some have not yet replied, and the addresses of a few others were indecipherable; but the 35 admissions which were not directly checked with the hospitals for these reasons have been confirmed again by further questioning of the mothers, and we are satisfied that the information relating to them is now correct.

When the hospital and nursing-home records are compared with the accounts given by the mothers of the 151 children admitted to them, it appears that 70% of dates were remembered correctly to within a month of the actual time of admission. A further 19% were between two and six months out, and 11% were less accurate than this. A cluster of errors of twelve months suggests that some of the larger discrepancies arose from verbal or recording mistakes rather than from faulty memories. The admissions were as often antedated as post-dated, and Table IV shows that

TABLE IV.—*Ages of Admission to Hospital and Nursing-home*

Source of Information	Age at Admission (Months)				Total
	0–13	14–25	26–37	38–51	
Mother* ..	42	38	28	43	151
Records† ..	42	35	32	42	151

* As remembered by the mothers.
† As given by the institutions.

there is a remarkable similarity between the age distribution of admissions obtained for the same children from the records and from the mothers themselves.

The analysis of hospital admissions given in the next section was based in the first place on the mother's information. It was then repeated when the hospital records became available. None of the original conclusions has had to be altered in the light of this re-analysis, and it would seem that for relatively large samples of children satisfactory information on major conditions of ill-health may be collected by the questionary methods used in this survey. On the other hand, it would clearly be unwise to base discussions of the health of an individual child on information of this type.

The admission of a child to hospital is a major event in his life and in the life of his family, and it may be that less serious events are less well remembered. But for the information we have been able to check (covering such diverse subjects as weaning from the breast, immunization, and post-natal examinations) it seems that we can rely on mothers' memories to bridge even a two-year gap (Rowntree, 1950; Douglas, 1951).

(c) Hospital and Nursing-home Admissions

This analysis is limited to the hospital and nursing-home admissions of the surviving children. Those who died were excluded because it was seldom possible after their death to question their parents about their past illnesses. Thirty-nine of the surviving pairs also were left out because information was lacking for one or both of them; among those excluded were five premature children and three controls who had been admitted to hospital but were paired with children whose mothers failed to answer the questions on hospital care. Accordingly there are 435 surviving pairs for whom we have information.

The fact that premature children are often retained in maternity hospitals for several weeks after birth is well known. In the present sample 39% of the surviving premature children, as compared with 11% of their controls,

were kept in hospital until they were more than 14 days old, the mean lengths of stay for all those born in hospital being respectively 17.7 days and 12.6 days ($t=6.91$, $n=593$, $P<0.001$). At this time maternity beds were in short supply, and it may be a reflection of this shortage that as many as 26% of the premature children sent home during the first fourteen days after birth weighed 5 lb. (2.3 k.g.) or less on leaving hospital. For this reason it is likely that the mean stay of 18 days found for premature children in this survey is an underestimate of their need for hospital care in the immediate post-natal period. Hospital stay directly related to labour or the special nursing needs of infants during the early weeks has been excluded from the following discussion for obvious reasons, and the figures given below refer with four exceptions (two premature children and two controls) to admissions occurring after the neonatal period.

Ninety-one premature children (21%) and 64 controls (15%) were admitted to hospital on at least one occasion during the first 4¼ years of their lives ($\chi^2 = 5.75$, $n = 1$, $0.02>P>0.01$). If the number of admissions is counted instead of the number of children admitted, then the proportions are respectively 26% and 17% in the two groups ($\chi^2=9.87$, $n=1$, $P<0.01$). In each instance the admission rates are significantly higher for premature children. Three of the premature children, but none of the controls, spent a great part of their first four years in hospital. (See footnote to Table XV.) One is a spastic microcephalic who was kept in hospital because there was nowhere else for him to go; the second has pulmonary tuberculosis; and the third has bilateral cataracts and is now totally blind. These three children alone received 1,520 days of hospital care, which is more than the total number of days spent in hospital by all the controls during the same period. It is also nearly half the total amount of care given to all the premature children. For the following description of hospital care we propose to exclude these three children, since the extent of their disabilities would otherwise obscure the pattern of hospital care among those who were less handicapped.

Table V shows the average number of days spent in hospital during different age periods by premature children and their controls.

TABLE V.—*Average Number of Days per Child Spent in Hospital at Different Ages (Excluding Maternity Care)**

Age (in Months)	Average No. of Days per Child (432 Pairs)		Significance (n=862)	
	Premature Children	Controls	t	P
0–12	1·54	0·39	2·59	<0·01
13–24	1·42	0·44	2·82	<0·01
25–36	0·62	0·68	0·21	0·9–0·8
37–51	0·79	0·69	0·39	0·7–0·6

* Three premature children permanently in institutions have also been excluded (see text).

During the first two years premature children spend on the average three and a half times as many days in hospital as their controls do, a total of 1,269 days as compared with 359 for the controls. In the third and fourth years there is no difference between them, the total stay being respectively 608 days and 595 days.

The average stay per illness tends to be greater among premature children; 48% of those admitted to hospital stayed there for more than two weeks, as compared with 36% of the controls ($\chi^2=4.40$, $n=1$, $0.05>P>0.02$). Moreover, the premature children during the first two years show a much greater variability in the time they spend in hospital. In the third and fourth year, on the other hand, there are no significant differences either in the average stay or in the range of variation of the length of stay for each illness. For the remainder of this section, therefore, we will consider only admissions in the first two years of life.

*For convenience the term "hospital admission" is used to include both hospital and nursing-home admissions.

Table VI shows that there is a marked relationship between the birth weight of premature children and the likelihood of their being admitted to hospital.

TABLE VI.—*Hospital Admissions in First Two Years by Birth Weight of Premature Child*

Birth Weight of Premature Child	% Admitted to Hospital			Significance (n=1)	
	Premature Children	Controls	No. of Pairs	χ^2	P
4½ lb. (2 kg.) or less	19·05	5·95	84	5·44	0·02–0·01
4½–5 lb. (2–2·3 kg.)	15·52	5·17	116	5·62	0·02–0·01
5–5½ lb. (2·3–2·5 kg.)	9·36	7·23	235	0·70	0·5–0·3

In each group the admission rate is lower for the controls, but the differences are significant only for premature children weighing 5 lb. (2.3 kg.) or less.

In Table VII the hospital admission rates of male and female pairs are shown separately. While premature children of both sexes tend to be admitted to hospital more often than their controls, the difference is significant only for the males. It is of interest that females, both premature and controls, are less likely to be admitted than are males.

TABLE VII.—*Hospital Admissions in First Two Years by Sex*

Sex	Hospital Admissions in First Two Years			Significance (n=1)	
	Premature Children %	Controls %	No. of Pairs	χ^2	P
Male	17·98	7·87	178	8·07	<0·01
Female	9·34	5·45	257	3·05	0·1–0·05

The excess of hospital admissions among premature children is no greater when they have resulted from pregnancies complicated by toxaemia or ante-partum haemorrhage. Nor is it greater among those born more than two weeks early than among those born nearer term.

Table VIII shows the causes of admission to hospital among premature children and their controls. In preparing this table successive attacks of the same type of disease—for example, pneumonia—were counted separately, whereas repeated admissions for continuing disabilities—for example, cataract, congenital dislocation of the hip—were treated as single incidents.

TABLE VIII.—*Causes of Admission to Hospital During the First Two Years*

	% Admitted for Specified Illnesses (435 Pairs)		
	Premature Children	Controls	
Bronchitis and pneumonia	3·22	0·69	($\chi^2=6·06$, $n=1$, $P<0·01$)
Other infections	2·99	2·76	
Cataract	0·69	Nil	
Inguinal hernia	1·38	0·23	($\chi^2=2·28$, $n=1$, $0·2>P>0·1$)
Epilepsy and convulsions	0·46	Nil	
All other illnesses ..	2·99	2·30	
Accidents	0·92	0·69	

A number of conditions are more common among the premature children than among the controls, but, considering them individually, only lower respiratory infections are significantly more common, 42% of the excess of hospital admissions being attributable to infections of this type. The greater occurrence in the sample of premature children with cataract, hernia, and convulsions is of interest in the light of previous work, but a very much larger inquiry would be needed for a profitable statistical analysis to be made.

The higher incidence of lower respiratory infections among premature children admitted to hospital does not necessarily imply that they are, as a group, more likely to contract these diseases. It might mean, for example, that

once they fell ill they were more severely affected. In the following sections, therefore, we will consider the total incidence of upper and lower respiratory infections, whooping-cough, and measles.

(d) Infections of the Upper Respiratory Tract

Our information on upper respiratory infection is limited to an estimate of the number of colds caught by the survey children in the three months preceding their second birthday and in the six months centring on their fourth birthday. These estimates, which were made by their mothers, are of unknown accuracy and have therefore been used only to separate those with reputedly constant or frequent colds from those who seldom or never had them.

Table IX shows that at both 2 and 4 years prematurely born children tend to have more frequent colds than their controls, though the difference is significant only in the younger age group. There are, moreover, among the premature children nearly twice as many who suffered from frequent colds in both years.

TABLE IX.—*Proportion of Children with Frequent Colds*

	Premature Children %	Controls %	No. of Pairs	Significance (n=1) χ^2	Significance (n=1) P
More than 2 colds between Dec., 1947, and Feb., 1948 ..	20·3	14·4	395	4·67	0·05–0·02
More than 3 colds between Dec., 1949, and May, 1950 ..	18·6	15·4	408	1·47	0·2–0·1
Frequent colds in both periods ..	6·4	3·8	344	2·44	0·2–0·1

(e) Lower Respiratory Infections

Our information on lower respiratory infections covers only the incidence of first attacks during the first two years of life which were treated by a doctor at home or in hospital. Accordingly the following figures are not directly comparable with those given for hospital admissions which include as separate illnesses successive attacks in the same child. Table X shows the mean incidence of first attacks of lower respiratory infections at different ages.

TABLE X.—*First Attacks of Lower Respiratory Infections Treated Either by a Doctor at Home or in a Nursing-home or Hospital*

Age at Attack (in Months)	Mean Monthly Rate per 1,000 Children Exposed (445 Pairs)		Significance (n=1)	
	Premature Children	Controls	χ^2	P
0–7	16·64	8·26	8·49	<0·01
8–13	33·33	18·43	9·92	<0·01
14–24	10·06	7·55	1·33	0·3–0·2
All ages	17·58	10·53	17·28	<0·01

During the whole of the first year there is an excess of bronchitis and pneumonia among premature children; in the second year the same trend is apparent but the differences are not statistically significant. Further subdivision according to the birth weight of the premature member of each pair (Table XI) shows that the greatest difference between the premature children and their controls is found in the groups of lightest weight. This relationship is of the same order as that found for hospital admissions.

TABLE XI.—*Lower Respiratory Infections by Birth Weight of Premature Child*

Birth Weight	Mean Monthly Rate per 1,000 Exposed for First Two Years			Significance (n=1)	
	Premature Children	Controls	No. of Pairs	χ^2	P
4½ lb. (2 kg.) or less..	27·78	7·94	92	21·88	<0·01
4½–5 lb. (2–2·3 kg.)..	15·49	9·87	118	3·15	0·1–0·05
5–5½ lb. (2·3–2·5 kg.)	14·58	11·96	235	1·29	0·3–0·2

Sex differences in the incidence of lower respiratory infections (Table XII) are similar to those for hospital admissions. In both sexes there is a higher incidence among the premature children, the difference being smaller for females.

TABLE XII.—*Lower Respiratory Infections by Sex*

Sex	Mean Monthly Rate per 1,000 Exposed for First Two Years			Significance (n=1)	
	Premature Children	Controls	No. of Pairs Exposed	χ^2	P
Male	19·52	10·83	187	9·89	<0·01
Female	15·75	10·35	258	6·32	<0·01

Lastly, we have related the incidence of lower respiratory infections to the length of gestation, and found that the excess of these diseases among premature children was just as great among those delivered two or more weeks early as among those delivered later than this.

(f) Whooping-cough and Measles

The proportions of children who during the first four and a quarter years of life suffered from whooping-cough or measles are shown in Table XIII. From these figures it appears that premature children are no more likely to contract these two diseases; nor does a closer examination of the data suggest that they are more susceptible than the controls to either of these diseases in early infancy.

TABLE XIII.—*Incidence of Whooping-cough and Measles*

	% Falling Ill During the First 4¼ Years			Significance (n=1)	
	Premature Children	Controls	No. of Pairs Exposed	χ^2	P
Whooping-cough ..	30·43	28·38	437	0·45	0·7–0·5
Measles	41·76	45·24	431	1·06	0·5–0·3

Discussion

While many papers on the physical growth and mental development of premature children have been published, few studies have been made of their health. Capper (1928) thought that during the first year a premature child has little resistance to infection of the respiratory tract, whereas after the first year his resistance is not unlike that of a mature child. Mohr and Bartelme (1934) likewise noted the frequent occurrence of respiratory infections, particularly colds, among the prematurely born. But in neither of these inquiries was there an adequate group with which to compare the premature children, though Mohr and Bartelme attempted to use brothers and sisters as controls. Owing to the difference in age between the siblings, however, no useful comparisons could be made.

Drillien (1948), studying a series of premature deliveries, found that the smaller premature infants were particularly susceptible to septic skin infections and discharging eyes. She followed up some of these children when they were age 1½–4½ years and compared their illnesses with those of a sample of children born in the same hospital at term. Her analysis is complicated by the varying ages of the children, and by the fact that she was able to trace only 40% of them. It remains, however, the most serious general study of the health of premature children that has so far been made. Nasopharyngeal and respiratory infections were found to be more common among premature children, who also had a significantly higher incidence of pneumonia and whooping-cough than their controls. For

measles and discharging ears, on the other hand, the controls were apparently the more susceptible. These differences were greatest in the first year and of little importance in the second.

Ferguson, Brown, and Ferguson (1952) report that nearly 25% of premature children in Glasgow received hospital treatment during the pre-school period, for conditions other than prematurity. The amount of hospital treatment was "high among infants who had weighed not more than 4½ lb. (2 kg.) at birth." It is difficult to interpret these observations, because corresponding figures for children born at term are not stated, and the standard of prematurity adopted appears to have been length of gestation rather than birth weight.

A specific defect that has been receiving increasing attention during recent years is retrolental fibroplasia, first described by Terry in 1952. It is said to affect 12% of surviving children of birth weight of 3 lb. (1.36 kg.) or less (Terry, 1945) and to account for more than a third of the blindness in young children in the U.S.A. (Reese, 1949). Its incidence is increasing and seems to be associated with changes in the post-natal care of small premature babies. In England few cases were recorded before 1949, and most of those recorded since have been among children cared for in premature baby units. There is some evidence that the increased use of oxygen is associated with this condition (Kinsey and Zacharias, 1949; Crosse and Evans, 1952). In the present series of premature children no instance of retrolental fibroplasia was recorded, and the three children with grossly defective sight were all of too high a birth weight for this condition to be a likely alternative diagnosis.

The results of the present inquiry confirm these earlier studies by showing that hospital admissions and both upper and lower respiratory infections are proportionately more common among premature children. They also answer the criticism that, since premature children are on the average drawn from poorer homes, the greater morbidity among them is a reflection of their environment rather than of any physiological or immunological deficiency. They show that these differences in ill-health persist even when the premature children are compared with controls drawn from similar homes. Moreover, the differences are just as pronounced among those who have been brought up in relatively favourable home environments. Thus it will be seen in Table XIV that the excess of colds and lower

TABLE XIV.—*Upper and Lower Respiratory Infection Among Premature Children and Their Controls in Two Social Groups*

Occupation of Father	% With Frequent Colds at 2 Years		% With Lower Respiratory Infections in First 2 Years	
	Premature	Control	Premature	Control
Professional or clerical worker	19·6	12·8	25·7	13·6
Manual worker ..	20·5	15·0	33·5	17·9

respiratory infections is as great among premature children coming from the families of professional and clerical workers as among those from the families of manual workers.

Upper and lower respiratory infections, as would be expected from previous studies, are more common among the children of manual workers, whether they are prematurely born or not; but the excess of illness among the premature children is of the same order of size in each type of family.

This inquiry also enables us to state in roughly quantitative terms the burden that premature children throw on the hospital services. Table XV gives the actual number of days spent in hospital by premature and control children of different ages.

While it is evident that in the first two years premature children need considerably more care than those born at

TABLE XV.—*Number of Days Spent in Hospital at Different Ages (Premature Children and Controls)**

Age	Premature Children	Controls	Difference
1st year { Maternity ..	5,279	4,016	+1,263
1st year { Other	657	169	+488
2nd year	612	190	+422
3rd ,, ...	266	296	−30
4th ,, ...	342	299	+43

* Three premature children who spent a great part of their first four years in hospital have been omitted, =1,520 hospital days (see p. 751).

term, they do not, in fact, make any great call on the hospital services. Related to the whole survey population and not only to their controls, they received approximately 8% of the total maternity hospital care, 11% of all hospital care in the first two years, and 3% in later years.

The above figures do not fully describe the special needs of premature children, for there are a number who, although living at home, are to a varying extent incapacitated and likely to be an enduring burden on their parents and the community. The question of mental defect and epilepsy will be considered in a later paper; we are here concerned only with physical defects. It may well be that some potentially disabling conditions have been missed by the relatively crude methods used in this survey and, if so, we may hope to make a more accurate statement of the disabilities of these children when the results of the school clinical examinations are available. In the meantime it appears that the only serious physical defect that is more common among premature children is impaired vision. While there is no child in this series of births suffering from retrolental fibroplasia—perhaps owing to the rarity in 1946 of oxygen therapy—there are three with congenital cataract, all of whom weighed more than 4½ lb. (2 kg.) at birth. Two of these children are now completely blind and the third has some sight. Among the control children, on the other hand, there is no instance of blindness or grossly defective sight. Gross congenital defects, other than cataract, are equally common among the surviving premature children and their controls. Of the former, two had spina bifida and one transposition of the viscera; of the latter, one had spina bifida, one a congenital heart lesion, and one congenital dislocation of the hip. Less severe congenital defects, such as hare-lip, webbed toes, etc., were also found as often in the one group as in the other. In view of the high mortality from congenital defects among premature children, this similar incidence in the premature and control pairs is unexpected.

Summary

676 live-born premature singletons drawn from one week's births in 1946 in 424 maternity and child welfare authorities have been matched with 676 children born at term during the same week and drawn from similar home environments. This paper describes the health and survival of these children during the first four years of their lives.

Apart from unavoidable losses from death and emigration, only eight pairs have fallen out of the inquiry.

The high mortality of premature children extends beyond the first month of life, and between the ages of 1 month and 4 years is largely accounted for by deaths from congenital defects and lower respiratory infections.

During the first two years premature children show a higher incidence of hospital admissions, many of which are for bronchitis and pneumonia. At later ages they are no more likely to be admitted than are children born at term.

Upper and lower respiratory infections, including those treated at home as well as those treated in hospital, are more common among premature children

during the first two years. This greater susceptibility to infection is found among premature children even when they are reared in an apparently favourable home environment.

In general, premature children—after they have reached the age of 2—appear to be as healthy as those born at term.

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REPORT OF TUBERCULIN SURVEY IN THE RHONDDA FACH

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The tuberculin test has long been recognized not only as a useful measure in clinical diagnosis but as an essential part of epidemiological investigations appertaining to tuberculosis (Ustvedt, 1942). Myers (1946) declares that "as an epidemiological agent, the test excels every other procedure of examination," and he regards repeated testing of special groups as an excellent method of determining the effectiveness of a tuberculosis control programme. Though a more accurate index of the success of such control measures is undoubtedly the number of new cases of tuberculosis occurring in a community subject to intensive and repeated mass *x*-ray surveys, the tuberculin-testing of large groups does provide evidence on the existing degree of total communal infectivity. It was therefore decided to carry out skin tuberculin-testing of the school population in the Rhondda Fach as an integral part of the research scheme.

This scheme has as one of its main objectives the determination of the total prevalence of pulmonary tuberculosis in a defined community, the isolation and treatment of all known active cases, and the estimation of the rate of occurrence of new cases subsequent to the application of such measures (Cochrane, Cox, and Jarman, 1952).

The schoolchildren in the Rhondda Fach were tuberculin-tested during the months of February, March, and April, 1951, and a sample of the schoolchildren in another valley were tested during September, 1951. When the Rhondda Fach is resurveyed radiographically in 1953 the school population will again be tuberculin-tested and the results of such retesting will be compared with those of the 1951 survey. A sample of the schoolchildren in the "control" valley, drawn from the same schools as were those in this 1951 survey, will also be retested in 1953, and the results will serve for comparison with those obtained from the Rhondda Fach.

Such retesting will be combined with a follow-up study of children who were tuberculin-negative in 1951, and this will permit a determination of the attack rate of infection in the two valleys.

Method of Testing

In 2,301 cases the usual Mantoux technique was employed : 0.1 ml. of a 1/10,000 dilution of standardized O.T.—that is, 1 T.U.—was injected intradermally, and all negative reactors were retested with 0.1 ml. of a 1/100 dilution—that is, 100 T.U. The criteria adopted for the reading of these tests was that any reaction producing less than 5 mm. diameter of induration was regarded as negative. The reactions were recorded as measurements in millimetres of induration wherever this was possible, even when they were less than 5 mm. and, qualitatively, negative tests.

In 1,109 cases the initial test used was the multiple puncture test, employing standardized, adrenalized O.T. This is a modification of the Finnish Trambusti (1928) test and that described by Chester Stewart (1928). The reason for using this method, and the possible source of error involved, are discussed later.

A preliminary report on the multiple puncture test has been made recently (Heaf, 1951). The test is performed as follows : a drop of undiluted adrenalized O.T. is spread over an area on the forearm about the size of a shilling by means of a sterilized platinum loop ; the multiple puncture instrument is then applied and pressed home ; any excess of O.T. is wiped away with cotton-wool and the test is read at the end of 48 hours. The criteria adopted for the reading of this test were as follows : 0=no reaction,

TABLE I.—*Results of Tuberculin-testing of School Children*

Age in Years	No. who Completed Tests	No. Positive to 1/10,000 O.T.	No. Positive 1/100 O.T.	No. Positive to Multiple Puncture Only	Total Positive	% Positive
			(a) Rhondda Fach			
3	97	2	3	1	6	6·2
4	208	4	4	4	12	5·8
5	263	9	8	7	24	9·1
6	294	13	12	10	35	11·9
7	323	12	30	10	52	16·1
8	348	15	14	12	41	11·8
9	251	14	23	21	58	23·1
10	296	16	40	24	80	27·0
11	313	31	31	29	91	29·1
12	334	23	36	49	108	32·3
13	255	23	39	29	91	35·7
14	280	38	48	31	117	41·8
15	78	11	16	4	31	39·7
16	43	9	12	—	21	48·8
17	21	5	7	—	12	57·1
18	6	3	3	—	6	100·0
	3,410	228	326	231	785	23·0
			(b) Other Valley			
3	16	2	1	—	3	18·8
4	56	2	3	—	5	8·9
5	96	1	3	—	4	4·2
6	83	3	5	—	8	9·6
7	112	9	5	—	14	12·5
8	115	6	9	—	15	13·0
9	104	13	7	—	20	19·2
10	139	21	7	—	28	20·1
11	179	34	19	—	53	29·6
12	232	40	22	—	62	26·7
13	225	41	27	—	68	30·2
14	203	53	26	—	79	38·9
15	111	39	19	—	58	52·3
16	58	11	3	—	14	24·1
17	26	7	5	—	12	46·2
18	10	3	2	—	5	50·0
19	3	1	1	—	2	66·7
	1,768	286	164	—	450	25·5