A STUDY OF PREMATURE BIRTHS IN HOSPITAL

by

Margaret Mary Kerr

M.B.,Ch.B.,D.C.H

A Thesis

Submitted for the Degree of M.D.

UNIVERSITY OF GLASGOW

September 1956.

C O N T E N T S

P R E F A C E

Those privileged to work in the Neonatal Department of a Maternity Hospital must agree that the care of premature babies is a fascinating subject and one to which much more attention is now being paid. But the death rate, particularly among the very small infants, remains depressingly high and now accounts for a large proportion of the infant mortality in the country. The part played by premature labour in the aetiology of stillbirths is also of great importance.

Accordingly, it was thought to be worth while to review in retrospect the premature births occurring in the Glasgow Royal Maternity and Women's Hospital during a four-year period and to consider the relative importance of the various factors concerned, with particular regard to the aetiology.

I wish to express my thanks to Professor D.F. Anderson, Dr. J. Hewitt and Emeritus Professor R.A. Lennie for permission to consult the records of patients under their care. I am very much indebted to Professor Stanley Graham, who suggested that this survey should be undertaken, for his encouragement and advice.

A preliminary analysis of the findings has been published in the Glasgow Medical Journal.

I N T R O D U C T I O N

"I am quite ready to admit that an immense improvement in the treatment of the young has taken place within the last fifty years, and that, as a consequence, the rate of mortality in infancy has been greatly reduced. But it is equally true that this mortality, although much smaller than formerly, still continues so excessive in amount as to demonstrate the necessity of still further improvement."

So wrote Andrew Combe in 1840 - Andrew Combe, M.D., Fellow of the Royal College of Physicians of Edinburgh, Physician Extraordinary in Scotland to the Queen, Consulting Physician to the King and Queen of the Belgians - in his book entitled "A Treatise on the Physiological and Moral Management of Infancy."

One hundred and fourteen years later we read in a leading article of the Lancet (1954): "In the past fifty years infant mortality in Britain has fallen by four-fifths. The reasons for its decline include the improvement in social conditions, in nutrition during pregnancy, in ante-natal and obstetric care, and in the treatment of infections such as pneumonia and gastro-enteritis. But the fall in mortality has been greater after the first month of life than in the neonatal period, when many infants still die from anoxia, prematurity and congenital defects: indeed there are considerably more deaths in the first month than in/

in the next eleven."

Titmuss (1943) maintained that the words "Infant Mortality" have a deceptive simplicity, for in fact they mask some of the most complex problems of human society. He further averred that "from all the available evidence it is clear that in neonatal mortality, as in infant deaths as a whole, (and indeed in most matters concerning man's development) we have a problem of multiple causation. But because the problem is multifactorial that does not mean that we cannot isolate the major determinants."

At a meeting of the British Paediatric Association, Graham (1935) demonstrated that neonatal mortality had been practically uninfluenced by modern welfare schemes and that the first month of life remained as dangerous to infants as it had been at the end of the nineteenth century.

In the United Nations Population Study on Foetal, Infant and Early Childhood Mortality (1954) it was pointed out that the factors which are mainly responsible for neonatal mortality have proved less amenable to public health control than have the infectious and nutritional diseases. "It is evident that in countries where infant mortality is low, future progress will depend on the discovery and application of methods for the prevention and control of congenital defects and premature birth and on further improvement in obstetrical procedures."

Until the middle of the nineteenth century no attempt had/

had been made to review the incidence and causes of death among the population of Scotland as a whole, although Bills of Mortality had been prepared for many years from Parish Registers. These, unfortunately, were seldom accurate and rarely stated the cause of death. (Ferguson, 1948). Since the Registration of Births, Deaths and Marriages (Scotland) Act of 1854, however, the Registrar-General has been required to submit an Annual Report on the Vital Statistics of the country, the first of which, published in 1861, referred to the year 1855.

A study of these reports shows that, although the total death rate in Scotland declined steadily from about 1875, there was no corresponding decrease in the number of deaths among infants. Any improvements in the general standard of living produced by industrial development were not at first apparent in the homes of the poor, but were related to working conditions and to public sanitation. Indeed, the rapid extension of industries led to movement to the towns with increased over-crowding and the formation of new slum areas. Children at this time were too often regarded as encumbrances until they were old enough to be put to work. Smallpox was regarded as the "poor man's friend," since it took such a heavy toll of infant lives, thus saving the expense of up-bringing. Until 1800, this disease was known to be the greatest single cause of death among children in Glasgow. Thereafter,/

Thereafter, with the increasing popularity of vaccination, measles and scarlet fever became the killing diseases, frequently in severe epidemics.

From the foundation of the Town's Hospital in Glasgow, in 1733, many children received treatment there, but it was not until 1860 that the first hospital in Scotland solely for the treatment of children was opened. This was established in Edinburgh, where two years later, the first Medical Officer of Health was appointed. The Glasgow Royal Hospital for Sick Children was founded in 1882.

The eventual fall in infant mortality was closely associated with a better understanding of the problems of artificial feeding, but it was not until 1903 that the first depot was established in Scotland for the provision of sterilised milk for infants. This milk depot in Leith was followed in 1904 by similar centres in Glasgow and Dundee. About this time, too, health visitors were being appointed to visit the homes of the poor.

It became apparent at the beginning of the present century that not only had there been little decrease in the number of infant deaths, but that there had been a steady fall in the birth rate. Accordingly more attention was paid to the necessity of preserving infant lives. The October number of "The Practitioner" in 1905 was devoted to the/

the problems of infancy. The Editor commented: "The terrible waste of infant life has, of course, long been known to medical practitioners, but it is only recently that any serious anxiety has been aroused in the public mind." It was further stated that the chief cause of infant mortality was "not to be found in frailty of constitution." Eventually it was realised that the health of an infant was closely related to the wellbeing of the mother during her pregnancy and labour. In 1901, Dr. J.W. Ballantyne of Edinburgh published a paper entitled "A Plea for a Pro-Maternity Hospital", and in July of that year ONE bed was endowed in the Edinburgh Royal Maternity Hospital (founded in 1791) for the treatment of patients suffering from diseases of pregnancy. Hitherto pregnant women requiring hospital treatment had been admitted (with reluctance) to the wards of general hospitals. It was not until 1915 that an antenatal clinic for out-patients was established in Edinburgh - the first antenatal clinic in Great Britain. (Browne, 1955)

From these pioneer efforts have grown the Maternity and Child Welfare Services as they are today.

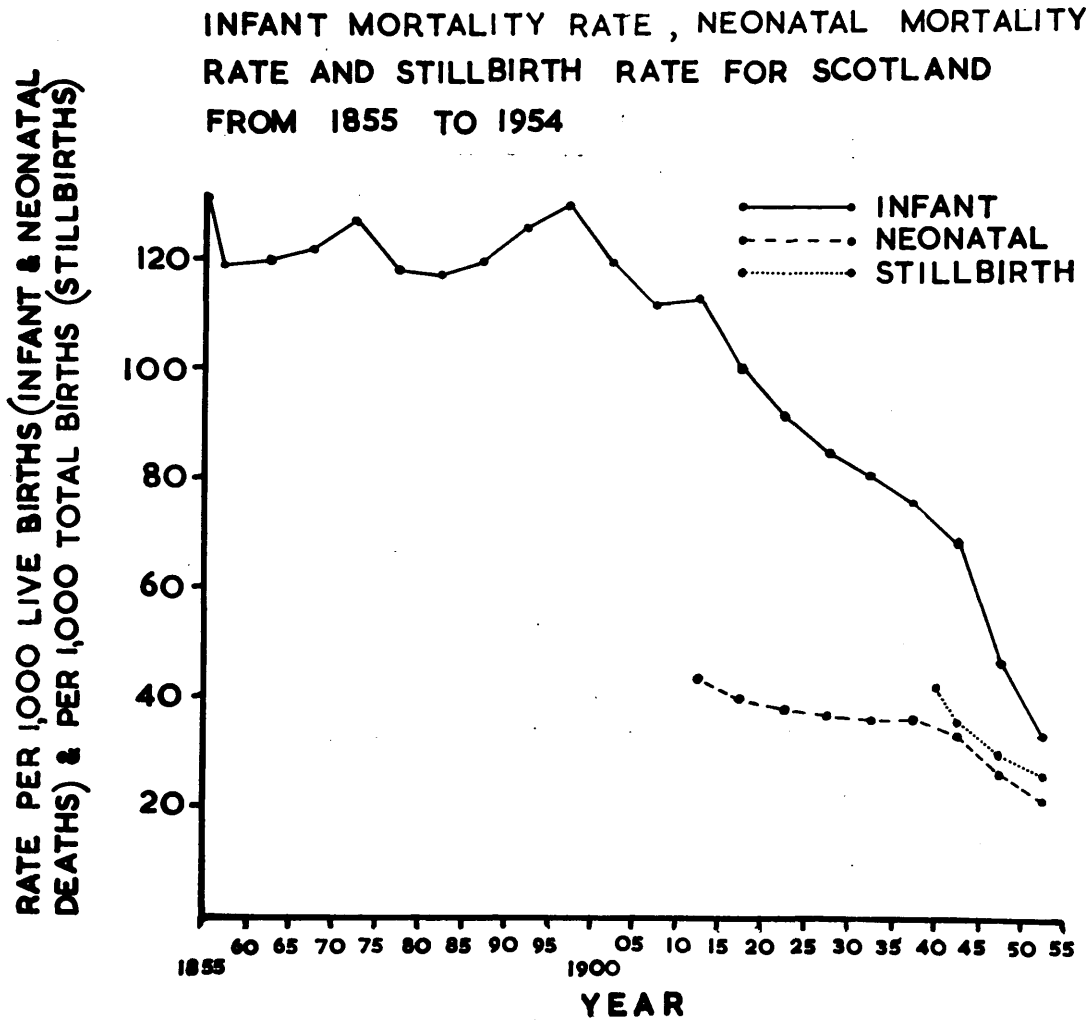
Although the infant mortality rates for Scotland are available from 1855, the neonatal mortality rate was not differentiated until 1911. The stillbirth rate for the country is known only from 1939, since until that year stillbirths/

stillbirths did not require to be registered. Figure I shows these three rates for each five-year period.

It is seen that the infant mortality, neonatal mortality and stillbirth rates are falling steadily but that the neonatal death rate now accounts for more than half the total infant mortality. According to the most recent Annual Report of the Registrar-General for Scotland, 1955, which refers to the year 1954, there were in that year 2,861 deaths of children under one year, of which 1,904 (66.6 per cent) took place in the first month of life. This infant mortality rate of 31.0 per thousand live births is the second lowest ever recorded in Scotland, being a fraction above the rate for the previous year. The stillbirth rate for 1954 was 25.3 per thousand total births, again the second lowest figure recorded for the country.

The reports do not state how many of the stillbirths and deaths occurred in premature infants, nor can this information be obtained for the country as a whole, since neither premature births, nor deaths of premature infants, are notifiable as such, and birth weights are not recorded on stillbirth certificates or on death certificates. Indeed, accurate birth weights are not readily obtained unless the infants are born in hospital. Nevertheless, a superficial study of any statistics related to stillbirth and neonatal death shows that premature birth is one of

FIGURE I


INFANT MORTALITY RATE , NEONATAL MORTALITY RATE AND STILLBIRTH RATE FOR SCOTLAND FROM 1855 TO 1954
RATE PER 1,000 LIVE BIRTHS (INFANT & NEONATAL DEATHS) & PER 1,000 TOTAL BIRTHS (STILLBIRTHS)
INFANT
NEONATAL
STILLBIRTH
120
100
80
60
40
20
1855
60 65 70 75 80 85 90 95
1900
05 10 15 20 25 30 35 40 45 50 55
YEAR

the most important factors concerned.

Ashby (1915), in a volume entitled "Infant Mortality", maintained that prematurity and "wasting" were responsible for about one-third of infant deaths and should therefore be regarded as "very important considerations". He was of the opinion that many of the so-called "non-preventable" deaths in infants could in fact be prevented "if the mother has instructions and is encouraged to look after herself more during the antenatal period. By doing so, many more infants would be carried to full-time and would grow up into healthy citizens."

It was not until 1923 that the first book on the subject of premature infants was published. "Premature and Congenitally Diseased Infants", was the work of Professor Julius Hess of the University of Illinois. His introduction may be quoted: "As part of the great movement towards conserving and developing the individual to his highest point of health efficiency, as an important factor in national health, and as an effort directed toward the source of a considerable morbidity, the care of premature infants and the conservation of their flickering lives has a prominent place."

In the report, "Infant Mortality in Scotland" (1943) which was concerned with the years 1934 to 1938, it was noted that prematurity was the most frequently stated single/

single cause of death in the first month of life and it was considered that its importance was greatly understated, since deaths were not assigned to prematurity if any other cause could be given. During the period reviewed in this report, West Central Scotland showed the highest infant mortality of any region in Great Britain, and the rate in Glasgow - 99 per thousand live births - was the highest of any city or large burgh in Great Britain. (Glasgow is notorious for this high rate. Titmuss (1943) wrote: "It is indeed an indictment of our social system when we find, for example, that in 1936 the infant mortality rate in Glasgow exceeded that for Chicago by 180 per cent, Oslo by 276 per cent and Stockholm by 290 per cent, and that it was in fact higher than the corresponding rates for Tokio, Buenos Aires and Montevideo.")

A joint committee of the Royal College of Obstetricians and Gynaecologists and the Population Investigation Committee undertook a survey of social and economic aspects of pregnancy and childbirth in Great Britain. This survey was concerned with all women delivered in England, Wales and Scotland during the week, 3rd. to 9th. March, 1946. The results of this investigation were published in "Maternity in Great Britain." (1948) The incidence of prematurity was found to be 6.4 per cent for single births, and the neo-

natal/

neonatal death rate among the premature infants was 204 per thousand live births. Of the total neonatal deaths in the survey, 52 per cent occurred in premature infants.

Douglas and McKinlay (1953), discussing the incidence or prematurity in Scotland in 1951, found premature births to be approximately 5 per cent of the total live births, and that 42.5 per cent of the deaths in the first month of life were in premature infants. They studied the mortality rates for infants under one month in Aberdeen, Dundee, Edinburgh and Glasgow, and found that for the premature infants the mortality was outstandingly heavy in Glasgow and Dundee, being 241 and 212 respectively per thousand live births.

Smith and Cook (1955) at a Round Table Discussion on the Special Problems of the Newborn gave the accepted incidence of premature birth as being approximately 7 per cent. Wallace (1953) showed that the incidence of prematurity in New York City has been rising. In 1939 it was 7.1 per cent and by 1949 it had risen to 8.2 per cent. Clifford (1955) described what he called an "interesting phenomenon" in the Boston Lying-in Hospital. Although the incidence of prematurity there has fallen among the private patients, it has been rising in the general wards - from 6.3 per cent in 1944 to 8.3 per cent in 1954.

Observations on the experiences in different centres are/

are obviously of value, and it was decided, therefore, to study the problem of premature birth and its mortality rates in relationship to the total number of births in the Glasgow Royal Maternity and Women's Hospital. A four-year period (1949 to 1952) provided adequate numbers and this thesis is concerned with trying to obtain the answers to certain questions.

Why is the baby born prematurely - or below the average in weight? What are his chances of survival? What factors - before, during or after birth - influence those chances? And, above all, what can be done to lessen the incidence of premature birth and to increase the chance of survival in those so born?

THE PRESENT INVESTIGATION

Henderson (1946) put forward a plea for the standardisation of the statistics of prematurity. He considered that the following seven conditions should be fulfilled in any survey:

1. A large number of infants.
2. Accurate weighing at birth.
3. Strict interpretation of the definition of live-birth.
4. Inclusion of all live-born infants with congenital malformations.
5. Definition of the weight range of viable prematurity.
6. Subdivision of the standard weight range into half-pound weight groups.
7. Separation of "booked" from "unbooked" cases.

DEFINITION

For the purposes of classification, the definition of prematurity accepted was that recommended by the International Committee at Geneva in 1937. According to this definition, any infant weighing 5½ pounds (2.5 kg.) or less at birth is considered to be premature, regardless of the gestation period. To get a complete picture of the problem of prematurity it is obvious that stillbirths weighing 5½ pounds or less must also be considered in the study. So-called "pre-viable" infants are of course included in the series/

series - 2.6 per cent of the premature babies born alive weighed less than 2 pounds at birth.

Despite such a definition, many difficulties arise in attempting to assess the true incidence of prematurity or in comparing statistical data from various centres. Some hospitals admit mainly normal or "booked" cases where the antenatal care has been under supervision - and indeed the interpretation of what constitutes a "booked" case can vary considerably and it not always made clear. Other centres deal largely with emergency cases, the majority of which have had little or no antenatal care. The incidence of prematurity is known to be lower in booked than in non-booked cases, related, as it is, in some measure to the amount and type of antenatal care, but social and economic factors and maternal age and parity also exert their influence.

SOURCE OF MATERIAL

The Glasgow Royal Maternity and Women's Hospital contains eighty lying-in beds and admits a high proportion of abnormal cases. To consider some aspects of the cases dealt with, the latest Medical Report shows that in 1952, of the total of 5,090 admissions to the hospital, 2,085 (41.0 per cent) were classified as unbooked. A booked case, according to the classification adopted in the hospital, is one where the patient has attended the hospital's antenatal/

antenatal clinic on two or more occasions. This cannot be considered a satisfactory method of classification as far as the estimation of the adequacy of the supervision is concerned, and accordingly it was decided that the premature births to be studied could not be divided accurately into booked and unbooked. (Otherwise, Henderson's recommendations have been fulfilled.)

Of all the women delivered in the hospital during the years 1949 to 1952, 16.1 per cent were found to be suffering from the toxaemias of pregnancy. Delivery was effected by forceps in 11.0 per cent of all confinements and by Caesarean section in 6.2 per cent. The stillbirth rate in the hospital for these years was 62.3 per thousand total births as compared to a rate of 26.7 for the whole of Scotland. These figures will give some indication of the hospital patients providing the material from which the following statistics were obtained.

METHOD OF APPROACH

The weight of each infant born in the hospital is entered on the mother's case-record. These records are bound in volumes, each containing the consecutive admissions to the hospital for a period of half a calendar month. To ensure that all premature births were indexed, every case-record for the years 1949 to 1952 was inspected, thus information/

information was obtained concerning all premature infants born during these years. The majority of the live-born infants were admitted to the Paediatric Unit and for these babies separate record cards were available. A few of the more robust infants, weighing over 5 pounds, were nursed beside their mothers in the lying-in wards. Autopsy reports on still-births and neonatal deaths are included in the maternal case-sheets, so this information was available in relevant cases. The premature infants born in the hospital in the year 1939 were also indexed in the same way, as it seemed probable that interesting comparisons might be made. It should be noted that this series is concerned only with infants born in the hospital, as the accommodation in the Paediatric Unit does not permit of infants born outwith the hospital being admitted.

The relevant information for all premature infants born during these five years was recorded on punch cards, one being made out for each infant. The following were the facts recorded:

1. Case record number.
2. Name.
3. Maternal age.
4. Parity.
5. Date of delivery.
6. Method of delivery.
7. Duration of pregnancy in weeks.
8. Complications in the antenatal period.

9./

9. Complications during labour.
10. Type of sedation during labour.
11. Type of analgesia during labour.
12. Type of anaesthesia during labour.
13. Live birth.
14. Stillbirth.
15. Neonatal death.
16. Birth weight of infant - in pounds and kilograms.
17. Sex.
18. Whether admitted to Paediatric Unit.
19. Duration of stay in Paediatric Unit.
20. Occurrence of infection or other complications.
21. Presence of congenital abnormality.
22. Method of feeding.
23. Special treatment.
24. Age at death or dismissal.
25. Cause of death or stillbirth.
26. Any other relevant information.

To facilitate analysis, numerous sub-divisions were arranged, each being afforded a particular number or letter on the punch cards. In all, 2,567 cases were indexed in this way.

In the tables throughout the text, percentages are shown in brackets and have been corrected to the first decimal place.

INCIDENCE & MORTALITY RATES

INCIDENCE

During the four years chosen for review, (1949 to 1952) there were, including stillbirths, 13,396 infants born in the hospital and of these 1,955 (14.6 per cent) were premature. Of the 12, 561 live births, 1,519 (12.1 per cent) belonged to the premature group and of the 835 stillbirths, 436 (52.2 per cent) were classified as premature. Altogether 416 infants died - that is 3.3 per cent of the live births, and 302 (72.6 per cent) of these deaths were premature. These figures and the totals for the individual years are shown in Table 1. The corresponding figures for the year 1939 are also shown for comparison.

Particularly with the smaller prematures, it is often fortuitous whether the infant shows transient signs of life and is classified as a live birth and a neonatal death, or fails to show any sign of life and falls into the stillborn group. It is the sum of the stillbirths and the neonatal deaths - the perinatal mortality - which shows the true loss of potential lives. In Table 2 is given the perinatal mortality, calculated as explained above, for the same years - 1949 to 1952, with 1939 for comparison. This shows the extent of foetal wastage associated with prematurity for the present series to be 37.7 per cent as compared with 9.3 per cent/

TABLE 1

TOTAL BIRTHS, STILL BIRTHS, LIVE BIRTHS AND NEONATAL DEATHS ALL BIRTHS AND PREMATURE BIRTHS. 1939 and 1949 to 1952.

	ALL BIRTHS				PREMATURE BIRTHS			
Year	Total Births	Still Born	Live Born	Died	Total Births	Still Born	Live Born	Died
1939	3236	421	2815	215	612	163	449	146
1949	3221	233	2988	96	485	103	382	66
1950	3193	208	2985	107	508	114	394	78
1951	3330	204	3126	108	473	117	356	78
1952	3652	190	3462	105	489	102	387	80
Total 1949-1952	13396	835	12561	416	1955	436	1519	302

TABLE 2

PERINATAL MORTALITY

ALL BIRTHS AND PREMATURE BIRTHS.

1939, 1949 to 1952.

	ALL BIRTHS		PREMATURE BIRTHS	
Year	Total	Still Births and Neonatal Deaths	Total	Still Births and Neonatal Deaths
1939	3236	636 (19.7)	612	309 (50.5)
1949	3221	329 (10.2)	485	169 (34.8)
1950	3193	315 (9.9)	508	192 (37.8)
1951	3330	312 (9.4)	473	195 (41.2)
1952	3652	295 (8.1)	489	182 (37.2)
Total 1949-1952	13396	1251 (9.3)	1955	738 (37.7)

9.3 per cent for the total births. Although this rate is excessive it is noteworthy that in 1939 one half of the premature infants were either stillborn or failed to survive the neonatal period.

It is exceedingly difficult to find comparable figures from other institutions, either in this country or abroad - hence Henderson's plea for standardisation. Despite the generally accepted definition of prematurity, very few similar series are available for study. Frequently, figures quoted include infants born at home and transferred to hospital. In others, so-called pre-viable cases are excluded - that is, those infants whose birth weight is below 2 pounds or where the gestation period is considered to be less than 28 weeks. (This will obviously distort the picture.) Crosse (1952) in the appendix to "The Premature Baby" gives a most interesting series of tables from the Sorrento Maternity Hospital. For all except the first table, however, the statistics given refer to booked cases only. It is explained that the booked cases are by no means normal cases, but the exact definition of "booked" is not given. Russell and Betts (1952) discussed a ten-year study of 1,373 premature live births but mentioned that 98 per cent of the mothers were in the "upper income bracket". Bain, Hubbard and Pennell (1949) reviewed hospital fatality rates for premature infants but said that "for purposes of this study the term "fatality" is used to mean the deaths of premature infants occurring during/

during the time the infants were premature" - surely a rather unusual conception. Peckham (1938) published statistical studies on prematurity from Johns Hopkins Hospital. This series of over 4,000 infants covered the years 1896 to 1936. In it, however, were included infants born at home and transferred to the hospital and infants weighing less than 1500 G. or measuring less than 35 cm. at birth were not included.

However, Sandifer (1944) published an analysis of 1,000 consecutive cases of premature birth at Queen Charlotte's Maternity Hospital, London, these births taking place between April, 1936 and December, 1942. This series is in many respects similar to the present one. The incidence of premature birth was lower - 8.1 per cent of the total births compared with 14.6 per cent in the present series - but the stillbirth rate of 25.2 per cent, the neonatal death rate of 19.3 per cent and the perinatal mortality rate of 39.6 per cent are strikingly similar. There is, of course, a 13-year difference between the times of the two studies.

Many hospitals now publish Annual Reports following the recommendations of the Royal College of Obstetricians and Gynaecologists. These volumes contain a wealth of interesting detail. Table 3 shows the total births and premature live births and deaths for the year 1950 from nine maternity hospitals in Great Britain. Figures from the National Maternity Hospital, Dublin, are also included. It/

TABLE 3

TOTAL BIRTHS AND PREMATURE LIVE BIRTHS AND DEATHS FOR TEN MATERNITY HOSPITALS FOR THE YEAR 1950.

HOSPITAL	TOTAL BIRTHS	PREMATURES	
		Live Born	Died
Paddington Hospital, London	1977	112	12 (10.7)
Queen Charlotte's Hospital, London	2785	203	32 (15.8)
Nottingham Hospital for Women	829	85	19 (22.4)
Stobhill General Hospital, Glasgow	1548	146	32 (21.9)
University College Hospital, London	1284	*69	10 (14.5)
King's College Hospital, London	988	53	6 (11.3)
North Middlesex Hospital, London	2139	170	36 (21.2)
Mill Road Hospital, Liverpool	3411	289	35 (12.1)
National Maternity Hospital, Dublin	3828	+288	48 (16.7)
Glasgow Royal Maternity & Women's Hospital	3193	394	78 (19.8)

* Those over 28 weeks' gestation.

\+ Those weighing less than $2\frac{3}{4}$ pounds are excluded.

It is seen that there is a tremendous variation in the incidence of premature births and in the associated mortality rates, and the results, for reasons given above, are not strictly comparable.

However, the present series, while not in any way representative of the state of affairs pertaining in the general population or even in the average maternity hospital, may serve as a basis for enquiry into some of the problems of prematurity. It is obvious that a large series must be studied before conclusions can be drawn. The prematurity rate in the Glasgow Royal Maternity and Women's Hospital is certainly exceptionally high, but for that very reason an analysis should be of great help in elucidating some of the problems.

RELATIONSHIP OF BIRTH WEIGHT TO SURVIVAL

Other things being equal, the heavier the premature infant is at birth, the better will be his chance of survival. Table 4 groups the 1,519 live-born premature infants in this series according to birth weight, the number of deaths and percentage mortality being shown for each group, and Table 5 gives the total births and still-births for each weight group.

Considering the live-births, it is seen that the numbers in each group increase with the weight, as does the survival rate. That is to say, the neonatal mortality rate/

TABLE 4

LIVE BIRTHS AND NEONATAL DEATHS GROUPED ACCORDING TO WEIGHT.

BIRTH WEIGHT IN POUNDS	NUMBER OF LIVE BIRTHS	NUMBER OF NEONATAL DEATHS
Under 2 lb.	40	40 (100)
2lb. - 2lb. 7oz.	59	55 (93.2)
2½lb. - 2lb. 15oz.	67	60 (89.6)
3lb. - 3lb. 7oz.	82	42 (51.2)
3½lb. - 3lb. 15oz.	121	32 (26.4)
4lb. - 4lb. 7oz.	224	27 (12.1)
4½lb. - 4lb. 15oz.	296	25 (8.8)
5lb. - 5lb. 8oz.	630	21 (3.3)
	1519	302 (19.9)

TABLE 5

TOTAL BIRTHS AND STILL BIRTHS GROUPED ACCORDING TO WEIGHT.

BIRTH WEIGHT IN POUNDS	TOTAL BIRTHS	STILL BIRTHS
Under 2 lb.	71	31 (43.7)
2lb. - 2lb. 7oz.	98	39 (39.8)
2½lb. - 2lb. 15oz.	121	54 (44.6)
3lb. - 3lb. 7oz.	142	60 (42.3)
3½lb. - 3lb. 15oz.	187	66 (35.3)
4lb. - 4lb. 7oz.	286	62 (21.7)
4½lb. - 4lb. 15oz.	356	60 (16.9)
5lb. - 5lb. 8oz.	694	64 (9.2)
	1955	436 (22.3)

rate falls as the weight rises. This is shown in graph form in Figure II, which also shows the rate for 1939.

Franklin (1953) at a discussion at the Royal Society of Medicine on some problems of prematurity gave similar figures for a series of 739 infants from Queen Charlotte's Hospital, London, for the years 1948 to 1951. (This series is divided into four weight groups only - namely, 2½ pounds and less, 3½ pounds to 2½ pounds, 4½ pounds to 3½ pounds and 5½ pounds to 4½ pounds.) Crosse(1952) quoted a series of 426 infants born in the Sorrento Maternity Hospital, Birmingham, during the years 1947 to 1950. Her series, however, relates to booked cases only. The mortality rates for these two series and the present one are shown in Figure III. Brooks, Cass and Chinnock (1952) gave figures for the years 1949 and 1950 from Los Angeles County Hospital. This large centre deals with about 8,000 live births each year. Separate tables were given in their article for premature infants born within the hospital and for those admitted after birth. Brockway, Reilly and Rice (1950) analysed the monthly birth statistics for 1949 at King's County Hospital, Brooklyn. This was done with aim of comparing the statistics for Negro and White races but the totals are of interest. Figure IV shows the mortality rates from Los Angeles County Hospital, King's County Hospital, Brooklyn, and the series under discussion. (In this Figure the weights are expressed in kilograms.) All series show a similar trend although

in/

FIGURE II

NEONATAL DEATH RATE ACCORDING TO WEIGHT

1939 AND 1949 TO 1952

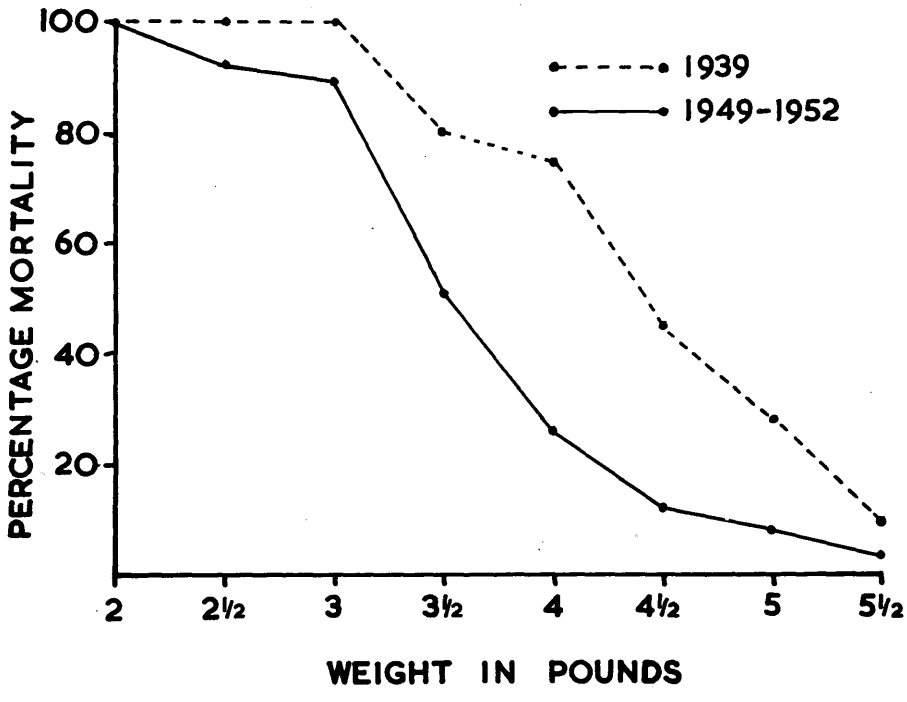


FIGURE III

COMPARISON OF NEONATAL MORTALITY RATES
QUEEN CHARLOTTE'S HOSPITAL, 1948 TO 1951
SORRENTO MATERNITY HOSPITAL, 1947 TO 1950
PRESENT SERIES, 1949 TO 1952

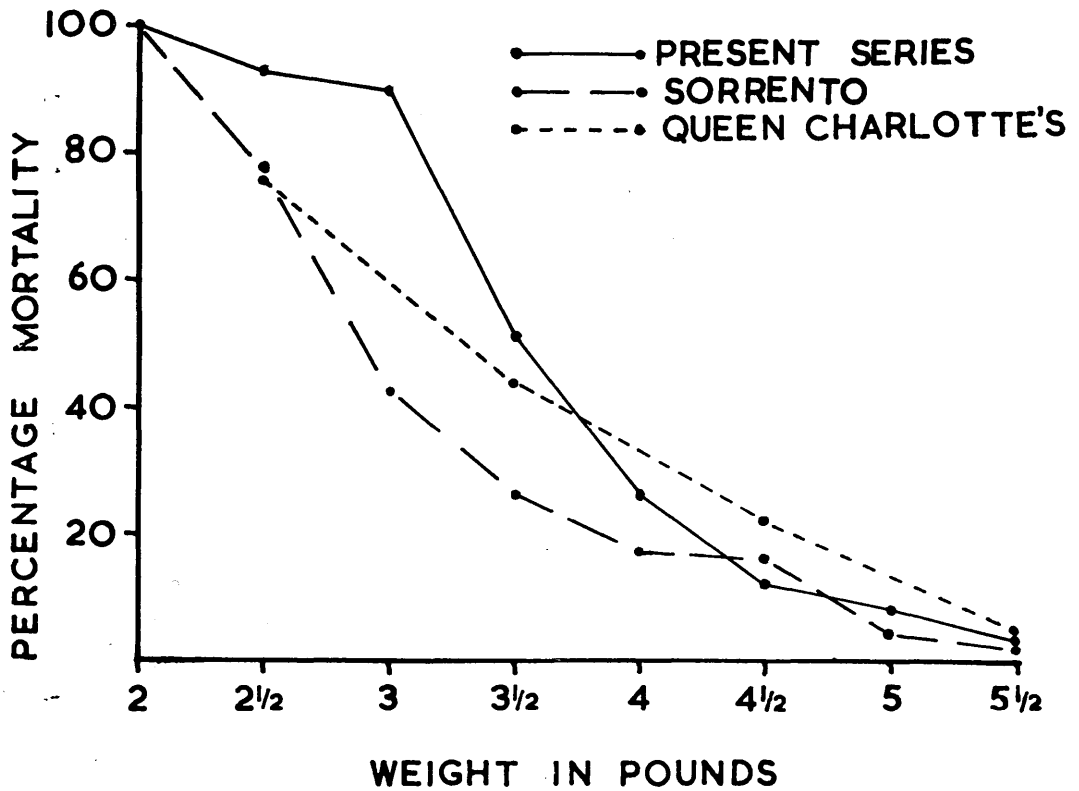
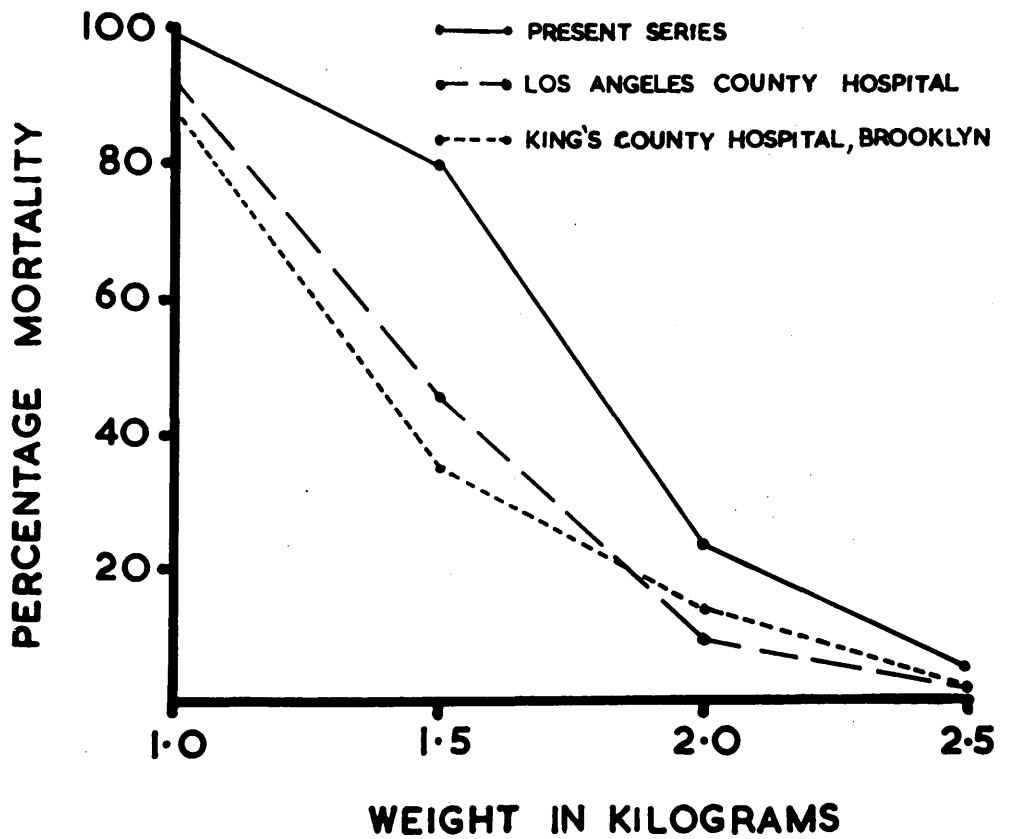


FIGURE IV

COMPARISON OF NEONATAL MORTALITY RATES FROM LOS ANGELES COUNTY HOSPITAL, KING'S COUNTY HOSPITAL, BROOKLYN, AND THE PRESENT SERIES



in the Glasgow group the mortality rate is slower to fall with increase in weight.

PERINATAL MORTALITY

As previously mentioned, however, the perinatal mortality rate gives a much truer indication of foetal wastage. Woolf (1946) maintained that stillbirths and neonatal deaths form a "natural aetiological grouping" and he considered that the influences common to both are foetal defects, unfavourable conditions in utero, the hazards of birth and adverse environmental circumstances. Wallace, Gold, Baumgartner, Losty and Rich (1954) pointed out that there is considerable evidence that many of the factors contributing to early neonatal death in premature infants may also be associated with premature stillbirths. They suggested that an artificial pattern has been used for many years - mainly for statistical purposes. With the smaller prematures, it is often a matter of chance whether a particular birth becomes classified as a stillbirth or an early neonatal death. Indeed Tyson (1946), in his series of 2,960 premature infants, with 618 deaths, reported that 164 infants (26.5 per cent of those dying) died in the labour ward, at ages varying from 5 to 60 minutes.

Although/

Although the term "perinatal mortality" as described herein has become generally accepted in recent years, Potter (1954) gave a rather unusual definition: "All products of conception weighing over 400 grams that have been born dead or that have died in the first ten days". Duncan, Baird and Thomson (1952) preferred the term "obstetric deaths" which they used to include stillbirths and deaths in the first week. But neither Potter's definition nor the term obstetric death seems as satisfactory as "perinatal mortality" and this term is now the accepted one.

In the series under review 738 infants were either stillborn or died in the neonatal period - 37.7 per cent of the total premature births. Table 6 shows this perinatal mortality according to weight group and Figure V is the corresponding graph in which is also shown the rate for 1939. As with the neonatal mortality rate, the perinatal mortality rate falls sharply with an increase in birth-weight.

Nevertheless, the overall figure of 37.7 per cent is alarmingly high, and represents a considerable loss of potential lives.

A critical investigation of these fatal cases ought to be of value from the point of view of prevention. But firstly it is essential to consider what factors may be concerned in the onset of labour before term - or in the birth of infants weighing 5½ pounds or less, whatever the gestation period.

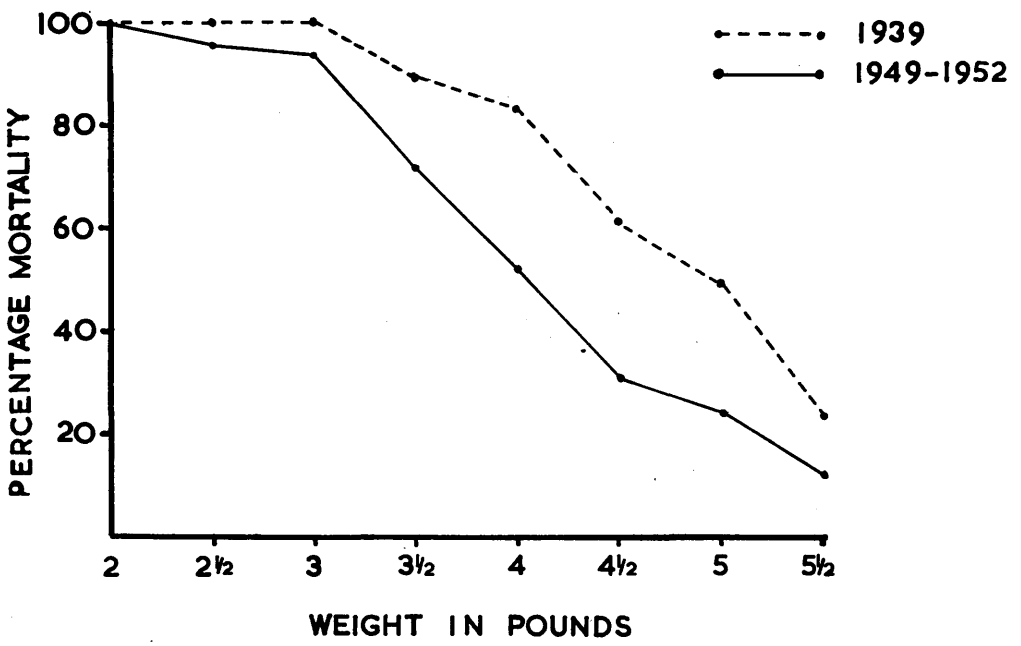
TABLE 6

TOTAL BIRTHS AND PERINATAL MORTALITY GROUPED ACCORDING TO WEIGHT

BIRTH WEIGHT IN POUNDS	TOTAL BIRTHS	PERINATAL MORTALITY
Under 2 lb.	71	71 (100)
2lb. - 2lb. 7oz.	98	94 (95.9)
2½lb. - 2lb. 15oz.	121	114 (94.2)
3lb. - 3lb. 7oz.	142	102 (71.8)
3½lb. - 3lb. 15oz.	187	98 (52.4)
4lb. - 4lb. 7oz.	286	89 (31.1)
4½lb. - 4lb. 15oz.	356	85 (23.9)
5lb. - 5½lb.	694	85 (12.2)
	1955	738 (37.7)

FIGURE V

PERINATAL MORTALITY RATE ACCORDING TO WEIGHT
1939 AND 1949 TO 1952



FACTORS CONCERNING THE BIRTH OF PREMATURE INFANTS

Morison (1952) reminded us that there is no single cause for premature birth. He stated that in the 35 to 70 per cent of cases which are often described as having a known aetiology all that should be inferred is an association with some abnormal maternal or foetal condition, such as the toxaemias of pregnancy, ante-partum haemorrhage, hydramnios or multiple pregnancy. He pointed out that reports of the incidence of these conditions vary considerably because such conditions as the toxaemias themselves vary in incidence in different parts of the world. Moreover, the assessment of their importance is subjective.

Eastman (1951) in his Fairbairn Memorial Lecture to the Royal College of Obstetricians and Gynaecologists on the "Causes and Management of Premature Birth", divided cases of prematurity into three main groups. The first group - about 12 per cent of all cases - he associated with multiple pregnancies. The second - about 13 per cent - were cases in which, because of some complicating factor, the pregnancies had been terminated prematurely by induction of labour or Caesarean section. There remained approximately 75 per cent of cases and these he said were still unexplained.

SOCIO-GENETIC FACTORS

It is indeed difficult to assess the importance of complications/

complications of pregnancy in causing premature birth, but it is even more hazardous to attempt to assess the part played by genetic and social factors. Yet it seems more than likely that such factors as social class, general nutrition of the mother, illegitimacy, employment of the mother - or unemployment of the father, housing conditions and maternal age and parity have an influence in the production of premature birth. Many workers have interested themselves in this aspect of the subject and there is a wealth of literature available for study.

In "Maternity in Great Britain" (1948) a brief analysis of prematurity was made. It was concluded that premature births may result from a number of biological and economic causes and that they cannot be explained by any single factor such as nutrition. During the course of this investigation into all births in England, Wales and Scotland during one week in 1946, information was obtained on the birth weights of 13, 257 single infants and on 338 multiple births. From these figures Douglas (1950) made a detailed analysis of the incidence and causes of prematurity for the whole country. Stillbirth rates were not given because 34 per cent of the stillbirths in the survey had not been weighed. Multiple births and illegitimate births were excluded. No information was available concerning the health and nutrition of the mothers during pregnancy.

It was confirmed that the incidence of premature birth is lowest among the well-to-do. But a significantly low incidence was found only in the most prosperous 9 per cent of the sample. It was shown also that the risk of premature birth did not rise with either increasing over-crowding or increasing family size, although over-crowding was shown to be associated with a rise in stillbirths and neonatal deaths.

Ferguson, Brown and Ferguson, (1952) reporting a retrospective study of premature infants born in the City of Glasgow during the years 1943 and 1944, found that over-crowding in the home scarcely influenced the neonatal mortality but had a definite effect on later mortality, being associated particularly with deaths from gastro-enteritis and pneumonia. Unfortunately, birth weight was not taken as the standard of prematurity in this series. The label "premature" had been affixed either on notification of the birth to the Medical Officer of Health or in Health Visitors' reports. In fact, 33.6 per cent of the infants in the study weighed over 5½ pounds at birth.

In the survey by Douglas, (1950) 8.3 per cent of first births were premature compared with 5.6 per cent of subsequent pregnancies. It was pointed out that the low incidence of premature birth in the professional and salaried classes occurred despite the fact that birth-spacing and maternal age were unfavourable.

It was shown in this survey that whereas the stillbirth rate/

rate (for all births) rose steadily with the mother's age, both the prematurity rate and the neonatal death rate were highest when the mother was 20 years or younger, both fell to a minimum at 26 to 30 years and thereafter rose again. It was also shown that there was no association of birth order with prematurity but that the birth interval was important. Whatever the mother's age, the incidence of prematurity was found to be consistently high with birth intervals of two years or less.

Thus both early childbearing and closely spaced pregnancies were found to be associated with a high risk of premature delivery.

It was demonstrated that, after standardizing for age and social class, premature delivery was associated with two important factors, infrequent antenatal supervision and heavy work during the last months of pregnancy, and it was thought not unlikely that the high risks of prematurity found in young working-class primigravidae were associated with these rather than with any physiological relationship between the age of the mother and the weight of her baby. This of course ignores the fact that frequently the weight of the baby is associated with a shortened gestation period - that is, with premature labour in the true sense. Although the period of gestation is not considered in the accepted definition of a premature infant, it is nevertheless

an/

an important factor, although one that does not lend itself easily to statistical investigation.

In the second part of his paper Douglas discussed antenatal supervision and work during pregnancy. After allowing for socio-economic differences and for the shorter duration of the pregnancies it was found that employment during the last four months of pregnancy was associated with a high incidence of premature birth. He also reported strong evidence that mothers of premature infants had been less regular in their attendances at antenatal clinics. He pointed out however, that the assessment of the significance of this is a most complex problem.

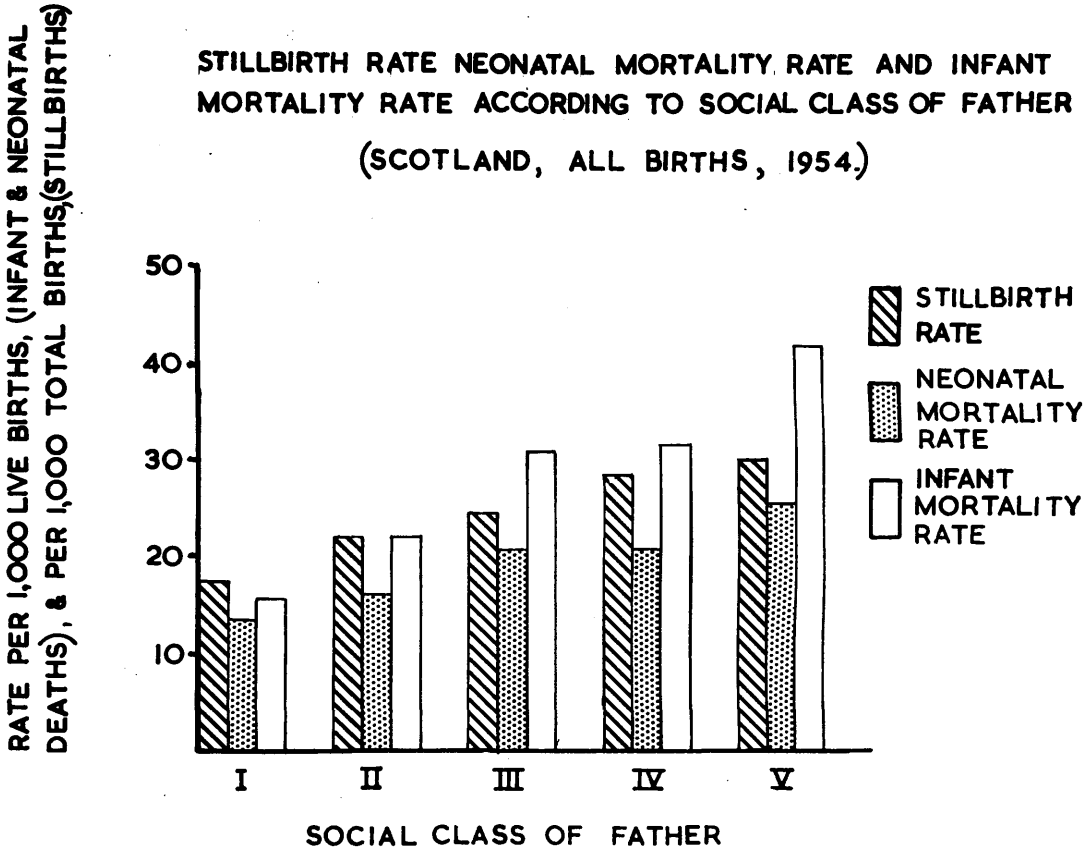
Baird (1945) discussed the influences of social and economic factors on stillbirths and neonatal deaths. He analysed three groups of cases occurring during the seven-year period 1938 to 1944, the variants being social class, place of confinement - hospital or nursing-home - and the type or standard of obstetric care - general practitioner or obstetrical specialist. (The hospital group were all "booked" cases.) There was a much higher incidence of prematurity in the hospital group (belonging to social Classes III, IV, and V) with an associated high neonatal mortality rate. The cause of the onset of premature labour was unexplained in about 50 per cent of cases in this group and Baird suggested that the most probable/

probable explanation was poor health and nutrition of the mother. In a later study, (1947), the same author found that the neonatal death rate attributed to prematurity in Social Class V was twice that of Social Class I.

However, Figure VI shows the stillbirth rate, neonatal mortality and infant mortality for Scotland for the year 1954 divided according to the Social Class of of the father. (Registrar-General's Report, 1955). It is seen that there is much less variation in the stillbirth and neonatal death rates than in the infant mortality rate - yet, the incidence of premature birth being much higher in Class V than in Class I, one would expect this to have a more pronounced effect on the stillbirth and neonatal death rates. Illsley (1955) suggested that selective interchange between classes at marriage tends to accentuate class differences and is partly responsible for the continuing disparity between the mortality rates for the various social classes. In this interesting study of married primiparae, he based the wife's social class on her father's occupation rather than on that of her husband. The highest prematurity rate was found among women in Social Classes I and II who had married men belonging to Classes IV and V.

Baird and his colleagues in Aberdeen (1952, 1953, 1954) have published a series of articles relating to the causes/

FIGURE VI


STILLBIRTH RATE NEONATAL MORTALITY RATE AND INFANT MORTALITY RATE ACCORDING TO SOCIAL CLASS OF FATHER
(SCOTLAND, ALL BIRTHS, 1954.)
RATE PER 1,000 LIVE BIRTHS, (INFANT & NEONATAL DEATHS), & PER 1,000 TOTAL BIRTHS,(STILLBIRTHS)
50
40
30
20
10
I
II
III
IV
V
SOCIAL CLASS OF FATHER
STILLBIRTH RATE
NEONATAL MORTALITY RATE
INFANT MORTALITY RATE

causes and prevention of stillbirths and first-week deaths. They pointed out that the wartime improvement in the stillbirth rate was a world-wide phenomenon and suggested that elimination of grosser forms of poverty, together with the provision of assured supplied of inexpensive and nourishing foods to expectant mothers in the United Kingdom was accompanied by a remarkable reduction in "obstetric" deaths. (The writers used the term "obstetric" deaths to cover stillbirths and deaths in the first week of life.) The reduction was mainly among obstetric deaths from ill-defined causes such as "congenital debility" and premature birth. They also reviewed the clinical records and statistical returns for the City of Abdedeen. They inferred that the reduction in stillbirths and neonatal deaths attributed to prematurity and "lack of vitality" which occurred both locally and nationally at the height of the war was due to full employment and an enlightened food policy, and declared that the elimination of physical ill-health and "physiological inefficiency" among women is largely a matter of national economic and nutritional policy.

The same authors classified the obstetric deaths occurring in Aberdeen Maternity Hospital during the fifteen-year period 1938 to 1952. This article concerned 1,008 infants. All were booked cases and multiple births were excluded. The classification was essentially clinical, and while one of the eight groups was designated "premature, cause unknown", this by no means included all the premature infants./

infants. For instance, babies weighing between 4 and 5½ pounds who died of birth trauma or infection were classified under these headings since they were not expected to die of immaturity per se. Nevertheless, the "premature, cause unknown" group accounted for 19.7 per cent of the total - the largest of the eight groups. The authors advanced the hypothesis that the high death rate in that group could be attributed to the effects of poor maternal health, poor physique and deficient diet during pregnancy.

Hellman (1953) speaking at a conference on Prematurity, Congenital Malformation and Birth Injury at the New York Academy of Medicine pointed out that numerous animal experiments have demonstrated foetal damage resulting from dietary deficiencies and said that there is a growing belief that premature labour can be traced in a large measure to defective maternal diet.

Some of these animal experiments were reviewed by Hugget (1946). He stated that there are two main pre-natal factors - the genetic and the nutritional - which will affect the chances of survival or improve the health of the infant.

Ebbs, Tisdall and Scott (1941), in what is now generally known as the Toronto Experiment, studied three groups of antenatal patients - those with poor diets, those/

those whose diets were initially poor but who were given adequate supplements, and those with good diets. The findings suggested that the nutrition of the mother influenced the whole course of pregnancy and directly affected the health of the child during its first six months of life. Of particular interest was the incidence or premature labour - 8.0 per cent in the group with poor diets as compared to 2.2 per cent and 3.0 per cent for the supplemented and "good" groups.

Cameron and Graham (1944) conducted an enquiry in the Glasgow Royal Maternity and Women's Hospital into the effect of maternal diet on stillbirths and premature labour. The first part of this enquiry was retrospective - data being collected in the puerperium about the diet during the last three months of pregnancy of three groups of patients - those with stillborn infants, those with prematurely-born infants and those with normal full-time infants. A significant difference was found in the superiority of the diets in the mothers of the full-time infants, particularly in regard to the intake of first-class protein, calcium and phosphorus. To test the validity of these findings they decided to supervise during the last three months of pregnancy the diets of a number of patients attending the hospital antenatal clinic, a control series being taken from the same clinic. It was found that there was a significantly lower incidence of/

of stillbirth and of premature birth in the group which had been under supervision.

A joint enquiry has been made into the Social and Biological Factors in Infant Mortality by the Social Medicine Research Unit of the Medical Research Council and the General Register Office, and a series of articles has been published. This enquiry was based on the 80,000 stillbirths and infant deaths which occurred among the 1½ million children born in England and Wales during 1949 and 1950. It referred of course to both mature and premature births. In the first article, (Morris and Heady, 1955) it was again pointed out that the underlying causes of deaths in the first month of life and particularly in the first week are similar to thoseof stillbirth. The authors averred that it is not at all clear how social influences affect the infant mortality rate and referred to the very numerous papers concerned with such factors. They suggested that no one or two factors have yet been incriminated in social class differences. In the second article, (Heady, Daly and Morris, 1955) they observed that the stillbirth rate rises with maternal age for any parity. In the third paper, (Daly, Heady and Morris, 1955) they demonstrated that social class differences in age and parity had little effect on the social class gradients of the three mortality rates - stillbirths, neonatal deaths and post-neonatal/

post-neonatal deaths. In the fourth paper, - Heady, Stevens, Daly and Morris (1955) - they showed that age, parity and social class are three distinct factors influencing mortality rates, the action of each being independent of the action of the other two. Regional differences were also discussed and again this factor was found to be independent of the other three. They stressed that this independence is not of course absolute - two factors may well reinforce or oppose each other in any particular case. The word "independent" is used in a defined sense - each factor exerts its own characteristic effect, whatever the values of the other factors.

In the Ministry of Health Report on Neonatal Mortality and Morbidity (1949) it is pointed out that the provision of proper living conditions for all sections of the community is insufficient unless the public are educated in the use of them - and also in wise spending add the provision of a balanced diet.

Discussing "reproductive wastage" in the United Nations Population Study (1954) it is maintained that "there appears to be a complex interplay between the various social and economic factors and the morbidity and mortality of young children within a given community. Family size and structure, housing conditions, nutrition, family income and the availability and proper utilization of adequate medical care are a few of the many determinants of/

of the frequency of early death. Conversely, morbidity and mortality within the family affect its size and its budget, and may significantly influence the productive capacity of its members and their impetus towards social and economic advancement."

To sum up, it is obvious that the cause of premature birth, in the majority of cases, is so far not understood. However, one fact of the greatest importance emerges - if the social and economic standards of the whole community were equal to those of Social Class I, the incidence of premature birth would be materially reduced. But such a Utopian state of affairs can never be brought about and obviously further study is required to define the various factors responsible and to assess their individual importance.

The following observations were made in the analysis of the present series of cases.

Social Class

It was unfortunately not possible in indexing the information available for this series to ascertain the social class of the mothers, nor could any assessment of their state of general nutrition be made. It has been mentioned before, however, that the hospital admits a large proportion of unbooked patients, many of whom come from overcrowded homes and are of poor intelligence. True poverty is now rarely encountered, thanks to higher wages/

wages and adequate allowances for the unemployed, but it is doubtful if the weekly income is used to the best advantage in many instances.

Maternal Age

Table 7 shows the premature live births and deaths grouped according to maternal age: no significant difference is to be noted. Table 8 gives the same information about the total births and stillbirths. As noted by other writers, there is a significantly high stillbrith rate for mothers aged 40 years and over, and this age factor is apparent in Table 9 which shows the perinatal mortality according to maternal age.

Parity

As regards the parity of the mother, Table 10 shows the live births and neonatal deaths grouped accordingly, and Table 11 shows the corresponding figures for total births and stillbirths. The perinatal mortality is similarly shown in Table 12. If the 12 cases in the two final groups are excluded, it appears that the perinatal mortality rises steeply with high parity. Presumably several factors are associated with each individual case. The highly parous woman tends to be older than the primigravida, her home may well be overcrowded and she may have had little time to seek antenatal care or may consider that she does not require it. Conversely,/

TABLE 7

LIVE BIRTHS AND NEONATAL DEATHS GROUPED ACCORDING TO MATERNAL AGE

	UNDER 20 YEARS	20-29	30-39	40 YEARS AND OVER
Number Born	78	827	546	68
Percentage of Total	5.1%	54.5%	35.9%	4.5%
Died	17 (21.8)	173 (20.9)	102 (18.7)	10 (14.7)

TABLE 8

TOTAL BIRTHS AND STILL BIRTHS GROUPED ACCORDING TO MATERNAL AGE

	UNDER 20 YEARS	20-29	30-39	40 YEARS AND OVER
Number Born	97	1026	717	115
Percentage of Total	5.0%	52.5%	36.7%	5.9%
Number Still Born	19 (19.6)	199 (19.4)	171 (23.8)	47 (40.9)

TABLE 9

TOTAL BIRTHS AND PERINATAL MORTALITY GROUPED ACCORDING TO MATERNAL AGE.

	UNDER 20 YEARS	20-29	30-39	40 YEARS AND OVER
Total Births	97	1026	717	115
Still Births and Deaths	36	372	273	57
Perinatal Mortality Rate	37.1%	36.3%	38.1%	49.6%

TABLE 10

LIVE BIRTHS AND DEATHS GROUPED ACCORDING TO MATERNAL PARITY

	PARITY				
	1	2 - 6	7 - 11	12 - 16	17 and over
Number Born	579	844	88	7	1
% of Total	38.1	55.6	5.8	0.5	0.1
Died	101 (17.4)	179 (21.2)	21 (23.9)	- -	1 (100.0)

TABLE 11

TOTAL BIRTHS AND STILL BIRTHS GROUPED ACCORDING TO MATERNAL PARITY

	PARITY				
	1	2 - 6	7 - 11	12 - 16	17 and over
Total Births	738	1081	124	11	1
% of Total	37.7	55.3	6.3	0.6	0.1
Still Births	159 (21.5)	237 (21.9)	36 (29.0)	4 (36.4)	-

TABLE 12

TOTAL BIRTHS AND PERINATAL MORTALITY GROUPED ACCORDING TO MATERNAL PARITY

	PARITY				
	1	2 - 6	7 - 11	12 - 16	17 and over
Total Births	738	1081	124	11	1
Still Births and Deaths	260	416	57	4	1
Perinatal Mortality	35.2	38.5	46.0	36.4	100

Conversely, the primigravida may be living in a sub-let single room, she frequently continues in her employment during her pregnancy and may have postponed attending the antenatal clinic although intending to do so once she ceases working.

COMPLICATIONS OF PREGNANCY

The association of soci-genetic factors with premature labour and premature birth have been reviewed at some length. The complications of pregnancy are now to be considered. In 827 of the 1,955 premature births in the series (42.3 per cent) no apparent complication was present during the pregnancy and there was no reason detected for the onset of premature labour. Morison (1952) stated that in 30 to 65 per cent of premature births no possible cause can be found even by the least critical writers.

The other cases have been divided into six groups. Where two factors were thought to be equally concerned the case was included under both headings. Table 13 shows the total births, stillbirths, live births, neonatal deaths and perinatal mortality grouped according to complications of pregnancy. The toxaemias of pregnancy and multiple pregnancy provide the largest groups, and these will be discussed in detail.

Hydramnios

This,/

TABLE 13

TOTAL BIRTHS, STILL BIRTHS, LIVE BIRTHS, NEONATAL DEATHS AND PERINATAL MORTALITY GROUPED ACCORDING TO ASSOCIATED MATERNAL FACTORS

	TOTAL BIRTHS	STILL BIRTHS	LIVE BIRTHS	NEONATAL DEATHS	PERINATAL MORTALITY
Multiple Pregnancy	430	51 (11.9)	379	82 (21.6)	133 (30.9)
Toxaemias of Pregnancy	444	160 (36.0)	284	49 (17.3)	209 (47.1)
Placenta Praevia	108	25 (23.1)	83	24 (28.9)	49 (45.4)
Hydramnios	102	67 (65.7)	35	15 (42.9)	82 (80.4)
Cardiac Disease	63	8 (12.7)	55	15 (27.3)	23 (36.5)
Miscellaneous Factors	164	46 (28.0)	118	20 (16.9)	66 (40.2)
No Apparent Associated Factors	827	104 (12.6)	723	136 (18.8)	240 (29.0)

This, the second smallest group, is associated with the highest perinatal mortality (80.4 per cent.) This condition is of course frequently associated with gross congenital abnormalities of the foetus, although the reason for this association has not yet been explained. It is also a frequent concomitant of plural pregnancy. Macafee (1950) put the incidence of hydramnios at about 1.25 per cent of all pregnancies and reviewed a series of 147 cases. 45.9 per cent of the infants in his series had some foetal abnormality, anencephaly being the commonest. The perinatal mortality was 55.5 per cent. These figures refer to total births - mature and premature - no weight groups being given.

Placenta Praevia

The perinatal mortality rate associated with placenta praevia is 45.4 per cent. Browne (1955) stated that 40 to 50 per cent of deliveries with placenta praevia are premature. He quoted figrues collected from the reports of eleven teaching hospitals in Great Britain as showing a foetal mortality rate of 54.2 per cent. This again included mature as well as premature infants. Murdoch and Foulkes (1952) reviewed the cases occurring in the Department of Obstetrics at Hammersmith Hospital. For the years 1942 to 1951 the foetal loss was only 13.1 per cent and for the last two years of the study - 1950 and 1951 - this had been/

been reduced to 6.9 per cent. In this series, however, the number of unbooked admissions was less than 1.5 per cent.

Macafee (1945) pointed out that one of the main causes of foetal wastage in cases of placenta praevia is prematurity and that this mortality can only be reduced by carrying on the pregnancy to as near term as possible. The foetal mortality for his series (1937 to 1944) was 23.5 per cent. Donald (1955) referred to Macafee's great contribution to the modern management of placenta praevia in that he advocated expectant treatment, thereby reducing the incidence of premature birth.

Cardiac Disease

Here the perinatal mortality is 36.5 per cent. Discussing serious heart failure in the later months of pregnancy, Browne (1955) stated that "fortunately, such patients tend to go into labour somewhat prematurely, or at least not to go beyond term." He also favoured surgical induction of labour after the 37th week provided cardiac compensation had been fully re-established. Donald (1955) however, stated that there is practically no place for induction of labour in the management of the patient with heart disease. He maintained that the infants are usually rather small and, that as a rule, the more serious the case, the more premature is labour likely to/

to be. Barry (1952) was also emphatic - "under no circumstances should there be any attempt to empty the uterus during failure. All are now agreed that this is a most dangerous procedure."

Miscellaneous Factors

This group, with a perinatal mortality rate of 40.2 per cent, includes cases of diabetes mellitus, severe anaemias, tuberculosis, rhesus incompatibility and acute febrile illnesses such as lobar pneumonia and acute pyelitis. Drillien (1947) found strong evidence that the chronic complications of pregnancy, e.g. cardiac disease, syphilis and anaemia, had an adverse effect on the birth weight but that the effect was not so well established nor of the same magnitude quantitatively as that observed with the toxaemias and antepartum haemorrhages. Her series from the Simpson Memorial Pavilion of the Royal Infirmary, Edinburgh, was drawn from booked, primiparous patients. Browne (1955) stated that there is a distinct tendency towards premature labour with pyelitis of pregnancy. This occurred with 30 per cent of his cases at University College Hospital and was thought to be attributable to high maternal temperature. As regards tuberculosis, it is generally stated that there is no tendency towards premature labour or abortion except where the tuberculous process is very acute.

Considering/

Considering rhesus incompatibility, Mollison, Mourant and Race (1952) stated that the infant with hydrops foetalis usually dies in utero at about the 34th week of pregnancy. Thereafter the onset of labour is usually premature due to the large size of the oedematous foetus and to the enlarged placenta. (The infant may of course be heavier than the premature weight limit.) Diamond (1947) had advocated induction of labour in sensitised patients with a rising titre of antibody. He suggested induction 2 or 3 weeks before term to minimize the risk of intra-uterine death. Mollison and Walker (1952) however, reporting the results of a controlled trial into the management and treatment of haemolytic disease of the newborn, found that while early induction certainly reduced the incidence of stillbirth, it led to a disproportionate increase in the number of neonatal deaths, and accordingly increased the perinatal mortality. Following this paper, induction of labour gradually went out of favour. The pendulum still swings, however, for Davies, Gerrard and Waterhouse (1953) suggested that, in selected cases, early induction is advantageous. They found in their series that if a previous child had been seriously affected then subsequent children would be similarily affected in 80 per cent of cases. They felt that it is therefore reasonable, in these circumstances, to practise premature induction - usually at the 34th to

36th week of gestation - unless the father is heterozygous. Walker and Murray (1956) were unable to demonstrate such distinctive family patterns, but during the last two years of their study had practised induction at 35 weeks in cases with a history of previous stillbirth due to haemolytic disease, where the father was known to be homozygous Rh positive.

The main hazard is of course kernicterus. The premature infant with icterus gravis is said to be more liable to develop this complication than the mature infant. Diamond (1947) believed that by immediate exchange transfusion the risk of kernicterus had been greatly diminished, but later he and his colleagues (Hsia, Allen, Diamond and Gellis, 1952) correlated serum bilirubin levels with the occurrence of kernicterus, and performed multiple exchange transfusions in order to keep the bilirubin level below 20 mgm. per 100 ml. Walker and Neligan (1955) considered that only a small proportion of cases required a second transfusion - but that it was mainly required in premature infants.

Multiple Pregnancy

Some authorities consider that one unsatisfactory aspect of the International definition of prematurity is that it does not allow for the reduction of individual weights in multiple births. A twin weighing 5 pounds is, generally/

generally speaking, at a more advanced stage of development than a singleton of the same weight, and many workers, in analysing premature births, have omitted multiple births from their series for this reason. But the advantage of the accepted definition is that any small infant, irrespective of the gestation period, will get the special care and attention he requires, whether he be a twin or not. From the statistical point of view, to reduce the weight or to omit twins would be cheating!

Cases of multiple pregnancy frequently go into labour before term and hydramnios is commonly associated with plural pregnancies. Donald (1955) suggested that the combination of plural pregnancy and hydramnios - even though it may be of mild degree - causes a degree of uterine overdistension sufficient to provoke the onset of premature labour in at least a third of cases. Accordingly it was decided to include multiple births in the general analysis of the present study and also to consider them as a separate group.

Four hundred and thirty infants in the series were the product of multiple pregnancies - an incidence of 22 per cent. Crosse (1952) gave the incidence as 17.2 per cent for all premature births in the City of Birmingham for the 12-month period from July 1948 to June 1949. Sandifer (1944) found the incidence to be 17.8 per cent in his series of 1,000 premature births at Queen Charlotte's Hospital,/

Hospital, London. Nixon (1953) gave the incidence as 15.5 per cent for University College Hospital, London, for the two-year period, 1951 to 1952.

Of the 430 infants in the present study, 51 (11.9 per cent) were stillborn. Of the 379 live births, 82 died (21.6 per cent.) The perinatal mortality rate was 30.9 per cent. Table 14 shows the total births, stillbirths, live births and neonatal deaths grouped according to weight. Table 15 contrasts the single live births and the multiple live births according to weight, the neonatal deaths also being shown. The total births and stillbirths for single and multiple pregnancies are shown.in Table 16, and finally, the perinatal mortality rates are contrasted in Table 17 and shown in graph form in Figure VII. It is seen that with those infants weighing 2½ pounds or more, the perinatal mortality rate is considerably lower in multiple pregnancy.

Crosse and Mackintosh (1954) gave corresponding figures for the city of Birmingham for 1952. (These of course refer to all premature births, not to a hospital population.) They stated that the fact that multiple born prematures have a lower perinatal mortality rate than the single born is largely due to the greater maturity of the multiple-born infant in relation to its birth weight.

Multiple pregnancy may of course be associated with complications/

TABLE 14

MULTIPLE BIRTHS - TOTAL BIRTHS, STILL BIRTHS, LIVE BIRTHS AND NEONATAL DEATHS GROUPED ACCORDING TO WEIGHT

BIRTH WEIGHT IN POUNDS	TOTAL BIRTHS	STILL BIRTHS	LIVE BIRTHS	NEONATAL DEATHS	STILL BIRTHS & DEATHS
Under 2 lb.	26	7	19	19	26
2lb. - 2lb. 7oz.	28	3	25	24	27
2½lb. - 2lb. 15oz.	24	3	21	18	21
3lb. - 3lb. 7oz.	24	6	18	6	12
3½lb. - 3lb. 15oz.	38	4	34	7	11
4lb. - 4lb. 7oz.	78	14	64	3	17
4½lb. - 4lb. 15oz.	97	10	87	4	14
5lb. - 5lb. 8oz.	115	4	111	1	5
	430	51	379	82	133

TABLE 15

LIVE BIRTHS AND DEATHS FOR SINGLE AND PLURAL BORN GROUPED ACCORDING TO WEIGHT

	SINGLE BORN		PLURAL BORN	
BIRTH WEIGHT IN POUNDS	LIVE BIRTHS	NEONATAL DEATHS	LIVE BIRTHS	NEONATAL DEATHS
Under 2 lb.	21	21 (100.0)	19	19 (100.0)
2lb. - 2lb. 7oz.	34	31 (91.2)	25	24 (96.0)
2½lb. - 2lb. 15oz.	46	42 (91.3)	21	18 (85.7)
3lb. - 3lb. 7oz.	64	36 (56.3)	18	6 (33.3)
3½lb. - 3lb. 15oz.	87	25 (28.7)	34	7 (20.6)
4lb. - 4lb. 7oz.	160	24 (15.0)	64	3 (4.7)
4½lb. - 4lb. 15oz.	209	21 (10.0)	87	4 (4.6)
5lb. - 5lb. 8oz.	519	20 (3.9)	111	1 (0.9)
	1140	220 (19.3)	379	82 (21.6)

TABLE 16

TOTAL BIRTHS AND STILL BIRTHS FOR SINGLE AND PLURAL BORN GROUPED ACCORDING TO WEIGHT

	SINGLE BORN		PLURAL BORN	
BIRTH WEIGHT IN POUNDS	TOTAL BIRTHS	STILL BIRTHS	TOTAL BIRTHS	STILL BIRTHS
Under 2 lb.	45	24 (53.3)	26	7 (26.9)
2lb. - 2lb. 7oz.	70	36 (51.4)	28	3 (10.4)
2½lb. - 2lb. 15oz.	97	51 (52.6)	24	3 (12.5)
3lb. - 3lb. 7oz.	118	54 (45.8)	24	6 (25.0)
3½lb. - 3lb. 15oz.	149	62 (41.6)	38	4 (10.5)
4lb. - 4lb. 7oz.	208	48 (23.1)	78	14 (18.8)
4½lb. - 4lb. 15oz.	259	50 (19.3)	97	10 (10.3)
5lb. - 5lb. 8oz.	579	60 (10.4)	115	4 (3.5)
	1525	385 (25.2)	430	51 (11.9)

TABLE 17

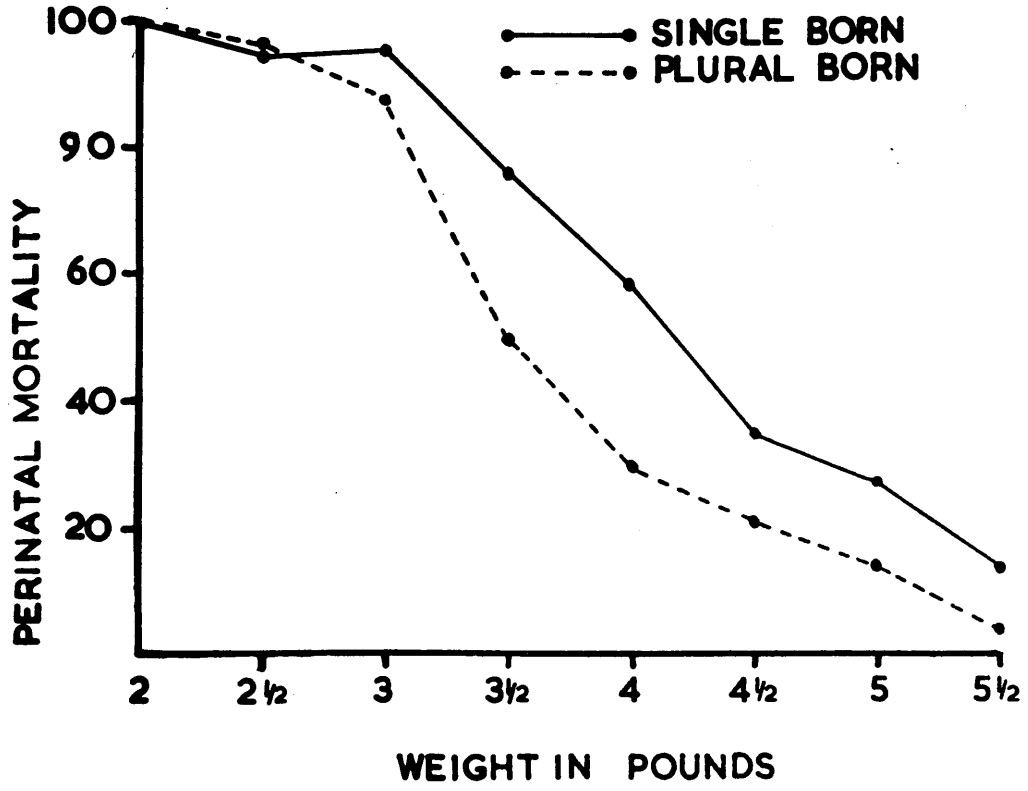
PERINATAL MORTALITY FOR SINGLE AND PLURAL BORN

GROUPED ACCORDING TO WEIGHT

	SINGLE BORN		PLURAL BORN	
BIRTH WEIGHT IN POUNDS	TOTAL BIRTHS	STILL BIRTHS AND DEATHS	TOTAL BIRTHS	STILL BIRTHS AND DEATHS
Under 2 lb.	45	45 (100.0)	26	26 (100.0)
2lb. - 2lb. 7oz.	70	67 (95.7)	28	27 (96.4)
2½lb. - 2lb. 15oz.	97	93 (95.9)	24	21 (87.5)
3lb. - 3lb. 7oz.	118	90 (76.3)	24	12 (50.0)
3½lb. - 3lb. 15oz.	149	87 (58.4)	38	11 (28.9)
4lb. - 4lb. 7oz.	208	72 (34.6)	78	17 (21.8)
4½lb. - 4lb. 15oz.	259	71 (27.4)	97	14 (14.4)
5lb. - 5lb. 8oz.	579	80 (13.8)	115	5 (4.3)
	1525	605 (39.7)	430	133 (30.9)

FIGURE VII

PERINATAL MORTALITY FOR SINGLE AND PLURAL BORN ACCORDING TO WEIGHT



complications of pregnancy. In 161 cases (37.4 per cent) one or more complications were present. These are shown in Table 18 with the corresponding total births, stillbirths, live births, deaths and perinatal mortality. The toxaemias of pregnancy were the most frequent complication - 78 cases, that is in 18.1 per cent of the multiple births. Russell (1952) reported this association in 20.4 per cent of his booked hospital cases (both mature and premature), and Bender (1952) gave the incidence as 24 per cent for similar material, although in his series an elevation of blood pressure was taken as the sole standard for the diagnosis of toxaemia. Aaron and Halperin (1955) however, found the association with toxaemia in only 5 per cent of their cases of multiple pregnancy.

The perinatal mortality is 25.6 per cent for multiple births associated with toxaemias as compared to 51.6 per cent for single births associated with toxaemias - a most striking difference. This lower foetal loss was also found by Bender. It may well be that a proportion of the cases classified as toxaemic are not in fact true toxaemias of pregnancy. In multiple pregnancy oedema can be explained - entirely or partly - as a result of pressure due to increased enlargement of the uterus and it is conceivable that a rise of blood pressure may be physiological. Albumenuria, however, is less easily accounted for.

The/

TABLE 18

MULTIPLE BIRTHS - TOTAL BIRTHS, STILL BIRTHS, LIVE BIRTHS AND NEONATAL DEATHS GROUPED ACCORDING TO ADDITIONAL ASSOCIATED MATERNAL FACTORS

	TOTAL BIRTHS	STILL BIRTHS	LIVE BIRTHS	NEONATAL DEATHS	STILL BIRTHS AND DEATHS
Toxaemias of Pregnancy	78	12	66	8	20 (25.6)
Placenta Praevia	12	2	10	4	6 (50.0)
Hydramnios	33	6	27	11	17 (51.5)
Cardiac Disease	17	1	16	6	7 (41.2)
Miscellaneous Factors	29	6	23	6	12 (41.4)
No Apparent Associated Factors	269	27	242	51	78 (29.0)

The other groups with associated complications are probably too small for comparisons to be made.

The method of delivery for the multiple births is considered in Table 19; the total births and perinatal mortality being shown. There is no significant difference between vertex and breech deliveries. The other categories are too small for comment.

Eighty-two of the infants died. No postmortem was performed in 5 cases. The autopsy findings are shown in Table 20 for the other 77 cases.

The high incidence of asphyxia and intra-cranial haemorrhage is noteworthy. One or other was found in 80.5 per cent of the cases on whom autopsies were performed. The significance of these pathological findings will be discussed later.

Bender stressed that the object of antenatal care in twin pregnancy should be to prevent as far as possible the premature onset of labour. He suggested that all cases should be admitted to hospital for bed-rest at the end of the 33rd week of gestation - or earlier in the presence of additional complications such as toxaemia. Russell advised admission at 30 weeks. Donald (1955) took a more practical view. He believes that unless the patient has had a series of obstetrical disappointments she is unlikely to be willing to go to bed for the last few weeks of her pregnancy. He suggested that cases of/

TABLE 19

MULTIPLE BIRTHS - TOTAL BIRTHS, STILL BIRTHS, LIVE BIRTHS AND NEONATAL DEATHS GROUPED ACCORDING TO METHOD OF DELIVERY

	TOTAL BIRTHS	STILL BIRTHS	LIVE BIRTHS	NEONATAL DEATHS	STILL BIRTHS AND DEATHS
Spontaneous Vertex	226	19	207	52	71 (31.4)
Breech	161	24	137	25	49 (30.4)
Forceps	22	4	18	2	6 (27.3)
Caesarean Section	18	2	16	3	* 5 (27.8)
Others	3	2	1	-	2 (66.7)

* Includes 3 quadruplets.

TABLE 20

MULTIPLE BIRTHS

AUTOPSY FINDINGS IN NEONATAL DEATHS

(82 Infants)

	No. of CASES
Asphyxia	31
Intraventricular Haemorrhage	16
Other Intracranial Haemorrhage	15
Atelectasis	-
Infection	11
Congenital Abnormality	-
Rhesus Incompatibility	2
Kernicterus of Prematurity	1
Others	1
"Prematurity"	3
No Autopsy	5

Where two factors were considered to be causal the case was included under both headings.

of triplets should however be strongly urged to co-operate in this matter.

The Toxaemias of Pregnancy

The toxaemias of pregnancy, comprising cases of pre-eclampsia, eclampsia and accidental haemorrhage, are frequently associated with the birth of premature infants. In the present series they form the largest group when complications of pregnancy are considered. Four hundred and forty-four of the 1,955 premature infants in the series were products of pregnancies complicated by toxaemia. Of these, 160 (36.0 per cent) were stillborn. Of the 284 born alive, 49 (17.3 per cent) died in the neonatal period, and this gives a perinatal mortality of 47.1 per cent. The total births, stillbirths, live births, neonatal deaths and perinatal mortality are shown in Table 21, where they are grouped according to weight. The loss of almost half the infants shows the seriousness of toxaemia as a complication of pregnancy. Table 22 shows the total births, stillbirths, live births, neonatal deaths and perinatal mortality for pre-eclampsia, accidental haemorrhage and eclampsia considered separately.

Browne (1950) stated that "the cause of stillbirth in pre-eclamptic toxaemia is placental infarction, with or without retroplacental haemorrhage. The retroplacental haemorrhage and consequent placental separation are believed/

TABLE 21

THE TOXAEMIAS OF PREGNANCY

TOTAL BIRTHS, STILL BIRTHS, LIVE BIRTHS, NEONATAL DEATHS AND PERINATAL MORTALITY GROUPED ACCORDING TO WEIGHT

BIRTH WEIGHT IN POUNDS	TOTAL BIRTHS	STILL BORN	LIVE BORN	DIED	PERINATAL MORTALITY
Under 2 lb.	10	10	-	-	10 (100)
2lb. - 2lb. 7oz.	19	11	8	5	16 (84.2)
2½lb. - 2lb. 15oz.	27	15	12	10	25 (92.6)
3lb. - 3lb. 7oz.	32	18	14	6	24 (75.0)
3½lb. - 3lb. 15oz.	58	28	30	8	36 (62.1)
4lb. - 4lb. 7oz.	80	25	55	7	32 (40.0)
4½lb. - 4lb. 15oz.	101	25	76	9	34 (33.7)
5lb. - 5lb. 8oz.	117	28	89	4	32 (27.4)
	444	160 (36.0%)	284	49 (17.3%)	209(47.1)

TABLE 22

PRE-ECLAMPSIA, ACCIDENTAL HAEMORRHAGE AND ECLAMPSIA

TOTAL BIRTHS, STILL BIRTHS, LIVE BIRTHS, NEONATAL DEATHS AND PERINATAL MORTALITY

	TOTAL BIRTHS	STILL BIRTHS	LIVE BIRTHS	NEONATAL DEATHS	PERINATAL MORTALITY
Pre-eclampsia	253	58	195	29	87 (33.6)
Accidental Haemorrhage	165	88	77	17	105(63.6)
Eclampsia	26	14	12	3	17 (65.4)

believed to be due to spasm of the spiral arteries of the decidua, causing anoxia of the capillaries distal to the spasm. When the spasm passes off and the blood flows again through the injured capillaries, they give way and retroplacental bleeding takes place. It is believed that this lethal degree of spasm of the spiral arteries is liable to occur if the systolic blood pressure exceeds 160 millimetres of mercury."

The toxaemias per se have a marked effect on lowering the birth weight, presumably due to placental damage and insufficiency, but the low weight is frequently related to the spontaneous onset of labour before term or to early termination of pregnancy either by induction of labour or by elective Caesarean section. Thus there are three groups of "toxaemic" babies:

1. Born at term.
2. Born after induction of labour, before term, or born by elective Caesarean section before term.
3. Born after the spontaneous onset of labour before term.

All, however, are probably suffering from the effects of placental insufficiency.

Brash (1949) found that the first group - those born at term - showed a higher incidence of stillbirth and neonatal death which she attributed to a liability to asphyxia - presumably associated with placental damage.

Drillien/

Drillien (1947), however, held that, while the toxaemias have a marked and significant effect in lowering the birth weight, there is no reason to suppose that they have any other consequence that can be measured by means of survival rates. Discussing the induction of labour she stated that it is of the utmost importance to carry the pregnancy on as long as possible, with due regard to the mother's condition. But Carey (1955) maintained that it is mainly the foetal prognosis which has to be considered - the risk of intra-uterine death being balanced against the dangers of prematurity.

In the present series 248 infants (55.9 per cent) were born after spontaneous labours. Table 23 shows the total births, stillbirths, live births, neonatal deaths and perinatal mortality according to the mode of termination of the pregnancy - spontaneous, by elective section or following induction by artificial rupture of the membranes or by insertion of bougies. The high perinatal mortality in the spontaneous group (53.2 per cent) is due to the large number of stillbirths in this group many of which were intra-uterine deaths occurring before the onset of labour. These figures would appear to argue very strongly against Drillien's contention.

There were 49 neonatal deaths among the infants born of toxaemic mothers, a mortality rate of 17.3 per cent. The autopsy findings are shown in Table 24. Again there is/

TABLE 23

THE TOXAEMIAS OF PREGNANCY

TERMINATION OF PREGNANCY

	TOTAL	STILL BORN	LIVE BORN	DIED	PERINATAL MORTALITY
Artificial Rupture of Membranes	147	37	110	23	60 (40.8)
Bougie Induction	19	7	12	1	8 (42.1)
Elective Caesarean Section	30	3	27	6	9 (30.0)
Spontaneous Labour	248	113	135	19	132 (53.2)

TABLE 24

THE TOXAEMIAS OF PREGNANCY

AUTOPSY FINDINGS
(49 Infants)

	NUMBER OF CASES
Asphyxia	20
Intraventricular Haemorrhage	8
Other Intracranial Haemorrhage	11
Atelectasis	-
Infection	12
Congenital Abnormality	1
Rhesus Incompatibility	-
Kernicterus of Prematurity	1
Others	-
"Prematurity"	2
No Autopsy	3

Where two factors were considered to be causal the case was included under both headings.

is a high incidence of asphyxia and intracranial haemorrhage in the fatal cases - 79.6 per cent - presumably associated in many instances with foetal anoxia due to placental insufficiency.

The management of the toxaemias creates many problems for the obstetrician. Satisfactory treatment must depend on a better understanding of the aetiology of the condition - although there is probably no other problem in obstetrics towards which more research has been directed. The accent must be on prevention and the importance of early and adequate antenatal care cannot be too highly stressed. This has been shown in Sydney where Hamlin (1952) reported a striking reduction in the incidence of pre-eclampsia and the eradication of eclampsia in booked cases at the Women's Hospital. The incidence in the Glasgow Royal Maternity and Women's Hospital is very high - as indeed it is in the West of Scotland generally; this high incidence can and must be reduced.

MODE OF DELIVERY AND MANAGEMENT OF LABOUR

Having considered the various factors which may be concerned in initiating premature labour, it now falls to examine the effects of labour and delivery on the infant.

MODE OF DELIVERY

With increasing awareness of the potentialities for survival among premature infants much more attention has been paid to the influence of the mode of delivery, and there is some controversy as to which is the safest method. Diddle and Plass (1942) stated that a spontaneous vertex delivery with an adequate episiotomy was probably safest although they agreed that a carefully performed forceps extraction entailed little or no additional risk. Beck (1946) also held that a spontaneous vertex, with episiotomy, under local anaesthesia, was the safest method. He pointed out the fallacy of drawing conclusions from over-all mortality rates compounded according to method of delivery, and maintained that the rates must be shown for separate weight groups. In his own series, this method showed that breech delivery was extremely dangerous whenever the child was under 2000 grams in weight. Drillien (1947) also found that breech delivery had a considerably greater wastage rate than

any/

any other method. She maintained that instrumental delivery was just as safe as spontaneous vertex delivery. But Eastman (1951) suggested that the use of forceps should be sparing.

Crosse (1954) stated that in her experience it is only among the larger premature babies that a spontaneous breech delivery becomes more lethal than a spontaneous vertex delivery. She pointed out other fallacies which arise; and stated that in assessing the influence of any mode of delivery on the mortality rates, it is essential to exclude births associated with other factors which might affect these mortality rates - factors such as multiple births, congenital malformations of the child and maternal complications of pregnancy. Thus the high mortality rate associated with premature infants born by Caesarean section is partly concerned with the complications necessitating this method of delivery.

All infants, live and stillborn, in the series are classified in Table 25 according to the method of delivery. The total births, stillbirths, live births, neonatal deaths and perinatal mortality are shown for each group. The small group designated "others" can be disregarded. It includes such abnormalities as partus corpore conduplicato and scalp traction with Willet's forceps. The highest foetal loss is associated with breech delivery. These cases were separated into assisted deliveries/

TABLE 25

METHOD OF DELIVERY

TOTAL BIRTHS, STILL BIRTHS, LIVE BIRTHS, NEONATAL DEATHS AND PERINATAL MORTALITY.

	TOTAL BIRTHS	STILL BIRTHS	LIVE BIRTHS	NEONATAL DEATHS	PERINATAL MORTALITY
Spontaneous Vertex	1402	288 (20.5)	1114	207 (18.6)	495 (35.3)
Breech	371	120 (32.3)	251	66 (26.3)	186 (50.1)
Forceps	54	8 (14.8)	46	9 (19.6)	17 (31.5)
Caesarean Section	111	5 (4.5)	106	19 (17.9)	24 (21.6)
Others	17	15 (88.2)	2	1 (50.0)	16 (94.1)

deliveries and manual deliveries and the perinatal mortality rates are shown according to weight in Table 26, which also includes the spontaneous vertex deliveries. Beck (1946) suggested that mortality rates for each method of delivery should be contrasted with the overall mortality for a series. Figure VIII shows this for spontaneous vertex, assisted breech and manual breech deliveries. It will be noted that the mortality is higher for manual breech deliveries in all weight groups.

The perinatal mortality rates for the present series and that of Diddle and Plass (1942) are shown together in Table 27. With the exception of the Caesarean section group the two series are remarkably similar - notwithstanding the fact that the American series commenced twenty-two years before the one under discussion.

The excessive foetal loss with breech deliveries in premature infants can be explained by the frequency of technical difficulty with the delivery of the after-coming head. The proportionately smaller breech does not dilate the cervix sufficiently to allow easy passage of the head. As with any breech delivery, the cord circulation becomes impaired during delivery and even this transitory anoxia may predispose to intracranial haemorrhage. In considering the cases of manual breech it must be remembered that this type of delivery is generally necessary because of some complicating factor such as ante-partum/

TABLE 26

METHOD OF DELIVERY

PERINATAL MORTALITY RATE FOR SPONTANEOUS VERTEX, ASSISTED BREECH AND MANUAL BREECH GROUPED ACCORDING TO WEIGHT

BIRTH WEIGHT IN POUNDS	SPONTANEOUS VERTEX 1402 cases	ASSISTED BREECH 270 cases	MANUAL BREECH 101 cases
Under 2 lbs.	100.0	100.0	-
2lb. - 2lb. 7oz.	95.5	100.0	100.0
2½lb. - 2lb. 15oz.	87.0	100.0	100.0
3lb. - 3lb. 7oz.	72.2	75.0	80.0
3½lb. - 3lb. 15oz.	54.9	46.7	54.5
4lb. - 4lb. 7oz.	25.5	36.4	45.5
4½lb. - 4lb. 15oz.	22.4	31.1	30.0
5lb. - 5lb. 8oz.	10.7	15.5	29.0
	35.3	51.5	46.5

FIGURE VIII

PERINATAL MORTALITY IN WEIGHT GROUPS

SERIES MORTALITY CONTRASTED WITH MODE OF DELIVERY

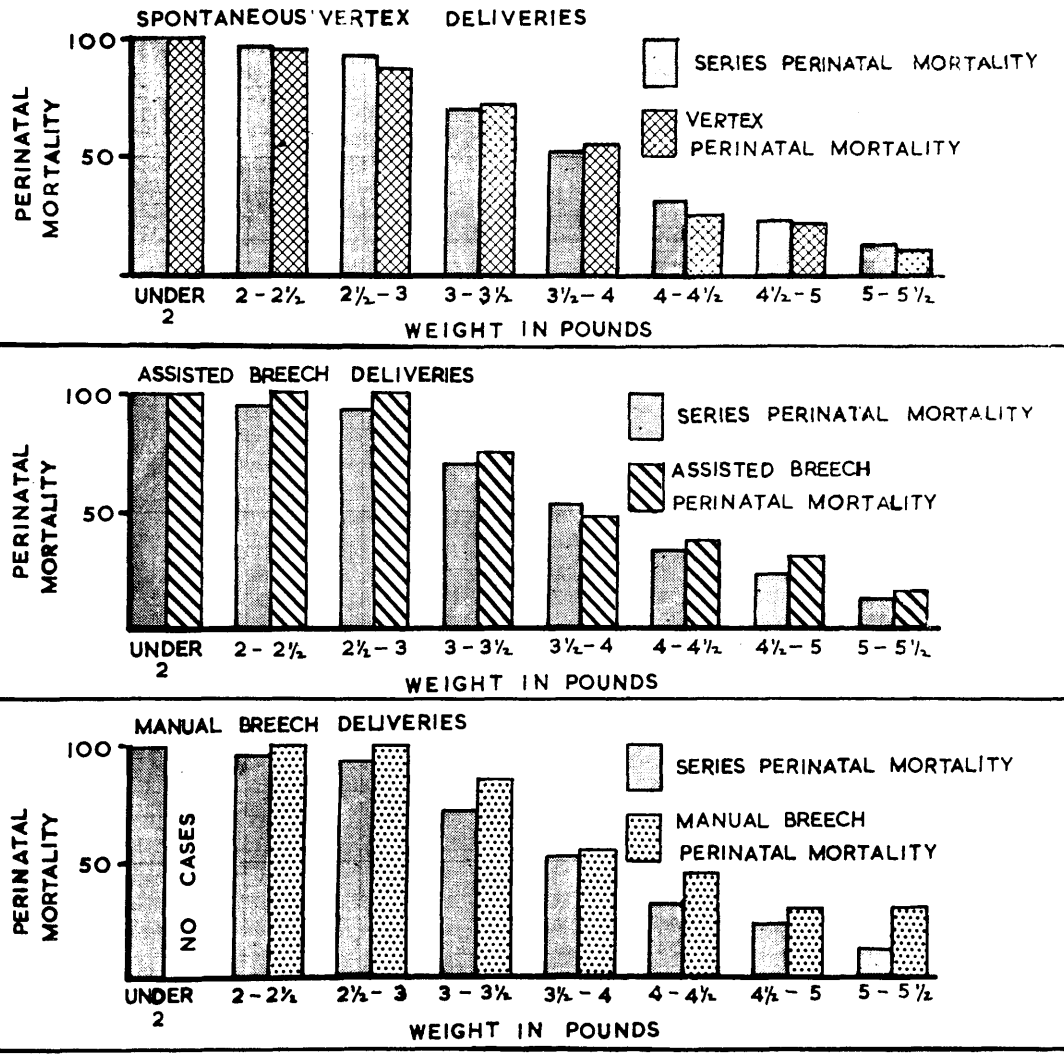


TABLE 27

COMPARISON OF PERINATAL MORTALITY ACCORDING TO MODE OF DELIVERY - PRESENT SERIES AND DIDDLE AND PLASS

	NUMBER OF CASES		PERINATAL MORTALITY	
	Present Series	Diddle	Present Series	Diddle
Spontaneous Vertex	1402	631	495 (35.3)	213 (33.8)
Breech	371	117	186 (50.1)	53 (45.2)
Forceps	54	60	17 (31.5)	18 (30.0)
Caesarean Section	111	21	24 (21.6)	11 (52.4)

NOTE. The weight range for Diddle and Plass was 700 G. to 2499 G.

Their series was from 1st July 1926 to 30th June 1941 and all sections were prior to July 1938.

ante-partum haemorrhage or a prolapsed cord, and that a general anaesthetic will have been required. Beck (1941) may perhaps be quoted here. Writing of premature infants he said: "In some instances the paediatricians have even gone so far as to tell the obstetrician how he should deliver these individuals. When such a state of affairs is reached, it is time for us obstetricians to review the situation seriously and correct our own shortcomings before those who are less competent attempt to correct them for us."

Fortunately there is now a growing interest among obstetricians regarding the welfare of premature babies and also a growing co-operation with their paediatric colleagues.

The autopsy findings are shown in Table 28 according to the method of delivery. The exact classification of "asphyxia," "intraventricular haemorrhage" and "other intracranial haemorrhage" will be discussed in the section concerning neonatal deaths.

ANALGESIA AND ANAESTHESIA

Almost every writer on the subject of the management of premature labour states that the administration of analgesic drugs and anaesthetics should be withheld or minimized, (Taylor, Phalen and Dyer, 1949, Bundesen, 1953, Cole (1954) and Donald, 1955) but, as Bourne and Williams (1948)/

TABLE 28

METHOD OF DELIVERY - AUTOPSY FINDINGS

302 cases

	SPONT. VERTEX	BREECH ASSISTED	BREECH MANUAL	FORCEPS	CAES. SECTION	TOTAL
Asphyxia	68	14	4	4	12	102
Intraventric. Haem.	53	8	4	-	1	*66
Other Intracranial Haem.	17	12	4	2	2	37
Atelectasis	6	-	-	-	-	6
Infection	38	7	1	2	2	50
Congenital Abnormalities	10	2	-	-	1	13
Rhesus Incompatibility	4	1	-	-	-	5
Kernicterus of Prematurity	4	-	-	-	-	4
Others	1	-	1	-	-	2
"Prematurity"	8	4	-	-	-	12
No Autopsy	10	4	1	1	2	18

* In addition, one infant delivered after application of Willett's Forceps.

(1948) remind us, every pregnant woman now expects something to be done for her relief during labour. Cole (1954) stated categorically that sedatives and general anaesthetics cannot be given to the mother without affecting the baby. Taylor, Scott and Govan (1951) and Taylor (1954) showed that the premature infant, during its first hour of life, is less able to oxygenate its blood in a fifty to sixty per cent oxygen atmosphere than is the full term infant. They suggested that this disability should not be further increased by drugs given to the mother. In view of recent knowledge on the aetiology of retrolental fibroplasia (Ashton, Ward and Serpell, 1953) this may even be considered too high a concentration for safety with the smaller infants. It is now generally accepted that infants weighing less than four pounds should not be given more than a 40 per cent concentration of oxygen and that the use of oxygen should be for as short a period as possible. It is now recognised that, although the very small infants may require to be nursed in incubators for days, or even weeks, it is neither necessary nor desirable to administer oxygen for more than a few days.

With regard to sedation and analgesia, Clifford (1953) may be quoted: "Those old enough to remember and young enough not to have forgotten, will recall that in the pre-analgesia-anaesthesia days of home delivery the need to resuscitate the product of a normal pregnancy and/

and delivery was a rare occurrence. Most of these babies cried lustily as they crossed the perineum."

Certainly pethidine and "gas" -and-air analgesia, properly used, have a minimal effect on the child, but effect there undoubtedly is, and with very small infants, or in the presence of an anoxia-producing complication, such as antepartum haemorrhage or interference with the cord circulation, the summation of the effects may lead to serious asphyxia. It is sometimes not appreciated, moreover, that a sedative can exert a harmful effect on the small infant while in utero - as well as at the time of its birth.

In America the conduction methods of relief of pain in labour have become popular in some centres (Masters and Ross, 1949) as has local anaesthesia, but these techniques have been slow to gain approval in this country. Certainly conduction anaesthesia requires a highly trained operator and much supervision, but more use might be made of local anaesthesia. As far as general anaesthesia is concerned, Clifford (1955) maintained that "under no circumstances should cyclo-propane be used because of the foetal anoxia it produces." There has been considerable controversy recently as to the ideal anaesthetic technique for use in obstetrics, (Crawford, 1956, Coleman and Day, 1956) and on this subject the Editor of the British Journal of Anaesthesia (1956) asks: "Who shall/

shall decide when doctors disagree?"

There is now available an antidote to pethidine and morphine in the form of n-allynormorphine ("Lethidrone" or "Nalorphine") which may be given to the infant at birth. But while this drug may have a dramatic effect in some cases, the situation can arise where, other factors being in operation, the cause of the anoxia may not be definitely attributable to the effects of the sedative.

With regard to the present series of infants, however, nalorphine was not available for use. The custom in the hospital was (and is) to make free use of sedatives and inhalation analgesia - the popular regime being the intramuscular injection of pethidine combined with gas-and-air analgesia. It has, unfortunately, not been found practicable to assess in retrospect the effect of the various drugs used on the condition of the premature infants in the series. However, only 180 cases of the 1519 live births in the study had no sedation, analgesia or general anaesthetic during labour. That is to say, 88.2 per cent had been given some form of medication.

Potter (1952) is of the opinion that in most reports dealing with the effects of analgesics and anaesthetics on the production of foetal anoxia, it is impossible to separate the effect of medication from other factors concerned with labour and delivery.

It would seem reasonable, however, to give minimal sedation during premature labour. Generally the patient herself will co-operate when the reason is explained to her. According to Judd (1954) the acceptance of discomfort will be met gladly in most instances. During the past few months this policy has been adopted in the Glasgow Royal Maternity and Women's Hospital. This is not a subject which can readily be investigated by means of a controlled series, but there has been general agreement that the results have been most gratifying.

PATHOLOGICAL CONSIDERATIONS

If progress is to be made, it is obviously of the greatest importance to ascertain the cause of death in stillbirths and neonatal deaths. But the observation and assessment of pathological and histological abnormalities in postmortem examinations of such cases requires considerable experience and there is not yet universal agreement on the significance of certain findings.

NEONATAL DEATHS

Of the 1,519 liveborn premature infants in the series, 302 died in the neonatal period, giving a neonatal mortality of 19.9 per cent. Autopsy examinations were carried out in 284 cases and the findings are shown in Table 29. Where more than one factor was thought to be concerned the cases were included under both headings.

In the classification adopted, cases designated "asphyxia" had no concomitent intracranial haemorrhage. Cases of intraventricular haemorrhage, although certainly associated with asphyxia, have been classified separately. The group recorded as "other intracranial haemorrhage" consists mainly of cases with subdural haemorrhage from tentorial tears, but includes a few cases of sub-arachnoid haemorrhage which may be either asphyxial or traumatic in origin. The group classified as "prematurity", with one/

TABLE 29

NEONATAL DEATHS - AUTOPSY FINDINGS

AUTOPSY FINDING	NUMBER OF CASES
Asphyxia	102
Intraventricular Haemorrhage	67
Other Intracranial Haemorrhage	37
Atelectasis	6
Infection	50
Congenital Abnormality	13
Rhesus Incompatibility	5
Kernicterus of Prematurity	4
Others	2
"Prematurity"	12
No Autopsy	18

one exception, is composed of infants weighing less than three pounds. "Others" consists of one case of liver necrosis and one of congenital syphilis. In Table 30 various categories are classified according to weight in pounds.

The autopsy findings will now be considered in detail.

Asphyxia and Intraventricular Haemorrhage

Signs of asphyxia were present in 102 cases and if the 67 cases of intraventricular haemorrhage are included, the total becomes 169 - or 56.0 per cent of all the autopsies. The weight groups for asphyxia and intraventricular haemorrhage are shown separately in Tables 31 and 32, and combined in Table 33. The age at death is of interest and is shown for the combined group in Table 34. It is seen that intraventricular haemorrhage was found mainly in infants weighing less than 4½ pounds. Also, if the two groups are considered together, 75.7 per cent of these deaths occurred within forty-eight hours of birth. The asphyxial process may be present before or during labour, or at birth, or may arise after birth in association with deficient pulmonary function. Potter (1952) observed that by far the most common cause of death in premature infants was abnormal function of the lungs, and that the smaller the infant the less was the pulmonary reserve/

TABLE 30

NEONATAL DEATHS

AUTOPSY FINDINGS GROUPED ACCORDING TO WEIGHT

	Under 2lb.	2lb.- 2lb.7oz.	2½lb.- 2lb.15oz.	3lb.- 3lb.7oz.	3½lb.- 3lb.15oz.	4lb.- 4lb.7oz.	4½lb.- 4lb.15oz.	5lb.- 5lb.8oz.	
Asphyxia	13	14	21	14	11	11	8	10	102
Intraventricular Haem.	12	17	13	9	8	5	3	-	67
Other Intracranial Haem.	5	6	5	4	3	6	3	5	37
Atelectasis	2	2	-	1	-	-	1	-	6
Infection	1	6	14	11	9	1	5	3	50
Congenital Abnormality	1	1	1	1	1	3	4	1	13
Rh. Incompatibility	-	-	-	2	-	-	-	3	5
Kernicterus of Prematurity	-	-	-	-	3	-	1	-	4
Others	-	1	-	-	-	1	-	-	2
"Prematurity"	3	5	3	-	1	-	-	-	12
No Autopsy	4	5	3	3	-	1	2	-	18

TABLE 31

CASES OF ASPHYXIA - WEIGHT GROUPS

Weight in Pounds	Under 2 lbs.	2 - 21b.7	2½ - 21b.15	3 - 31b.7	3½ - 31b.15	4 - 41b.7	4½ - 41b.15	5 - 51b.8oz.
No. of Cases	13	14	21	14	11	11	8	10

TABLE 32

CASES OF INTRAVENTRICULAR HAEMORRHAGE - WEIGHT GROUPS

Weight in Pounds	Under 2 lbs.	2 - 21b.7	2½ - 21b.15	3 - 31b.7	3½ - 31b.15	4 - 41b.7	4½ - 41b.15	5 - 51b.8oz.
No. of Cases	12	17	13	9	8	5	3	-

TABLE 33

CASES OF ASPHYXIA AND INTRAVENTRICULAR HAEMORRHAGE - WEIGHT GROUPS

Weight in Pounds	Under 2 lbs.	2 - 21b.7	2½ - 21b.15	3 - 31b.7	3½ - 31b.15	4 - 41b.7	4½ - 41b.15	5 - 51b.8oz.
No. of Cases	25	31	34	23	19	16	11	10

TABLE 34

CASES OF ASPHYXIA AND INTRAVENTRICULAR HAEMORRHAGE

AGE AT DEATH (169 cases)

Under 24 hours	24 - 48 hours	3 - 7 days	Over 7 days
83 (49.1)	45 (26.6)	38 (22.5)	3 (1.8)

reserve on which it could depend. Thus the premature infant is very liable to be affected by what may be called "the anoxic circle". Birth asphyxia, which may be due to several factors, depresses the cerebral respiratory centre and results in poor lung function which in turn prevents any improvement in oxygenation. Even if the infant is healthy at birth, intra-pulmonary complications are liable to develop and, with a sudden or gradual development of anoxia, lead to a depression of the vital cerebral centres.

Macgregor (1946) noted that intraventricular haemorrhage is an entity occurring almost entirely in premature infants. She found it most frequently in those dying on the first day of life and she suggested that the sub-ependymal haemorrhage is associated with birth asphyxia and that the rupture through the ependyma into the ventricular cavity is delayed for some hours.

Other Intracranial Haemorrhage

This was found in 37 cases and was generally subdural, in association with tentorial tears. Reference to Table 28 shows that it occurred in 16 cases of breech delivery and in 17 cases of vertex delivery.

Although bleeding from tentorial tears is generally ascribed to birth trauma, the process will certainly be encouraged by asphyxia with venous engorgement. Macgregor (1946)/

(1946) stated that it resulted directly from trauma but Potter (1952) thought it probable that the origin was asphyxial. Clifford (1953) stated that intracranial haemorrhage resulting from birth trauma has practically disappeared from modern obstetric practice.

Again the process is not clear - since asphyxia with venous engorgement will encourage haemorrhage, and primary haemorrhage will tend to initiate a state of asphyxia, there must often be a vicious circle created. Certainly, tears in the tentorium may be found at autopsy with minimal haemorrhage and, on the whole, it would seem highly probably that if haemorrhage occurs, asphyxia has been present.

Subarachnoid haemorrhage - unless as an extension of gross ventricular haemorrhage - is generally of minor degree and is said by Potter (1952) to be due to extravasation of cells in the areas around the major blood vessels.

It may be physiologically acceptable, then, to consider these three groups - asphyxia, intraventricular haemorrhage and other intracranial haemorrhage - as one, with anoxia as the common factor, and this combination is now referred to as the asphyxial group. Table 35 shows the weight distribution for the group of 206 cases and Table 36 gives the age at death. It is then seen that 50 per cent of these cases are associated with deaths occurring/

TABLE 35

ASPHYXIAL GROUP - WEIGHT GROUPS

(206 cases)

Weight in Pounds	Under 2 lbs.	2lb.- 2lb.7	2½ - 2lb.15	3lb.- 3lb.7	3½ - 3lb.15	4lb.- 4lb.7	4½ - 4lb.15	5lb.- 5lb.8oz.
No. of Cases	30	37	39	27	22	22	14	15

TABLE 36

ASPHYXIAL GROUP - AGE AT DEATH

Under 24 hours	24 - 48 hours	3 - 7 days	Over 7 days
103 (50.0)	55 (26.7)	45 (21.8)	3 (1.5)

occurring during the first twenty-four hours after birth and a further 26.7 per cent with deaths on the second day. In only 3 cases had the infants survived for longer than seven days and in two of these cases there was a concomitant broncho-pneumonia, which possibly was the lethal process.

Atelectasis

This is not now regarded as a cause of death but is considered to be the result of other pathological processes - Potter and Adair (1939). Smith (1946) maintained that the use of the term atelectasis had only caused confusion since "the lungs of all infants must be atelectatic at birth and persist in being more or less so for varying periods of time". He considered that the distinction between physiological and pathological atelectasis could only be drawn with difficulty and "perhaps had best not be drawn at all". Potter (1953) may be quoted: "Atelectasis is a descriptive term indicating the absence of air in the lungs, but it is not a diagnosis of a pathological entity and as such should not be considered a specific cause of death."

Mention may be made here of hyaline membrane. It seems strange indeed, writing in the year 1956, to find no mention of this fascinating condition when attempting to classify a series of neonatal deaths in premature infants.

Claireaux/

Claireaux (1953) found the membrane in 29 per cent of a series of neonatal deaths and Potter (1952) held that it was the most important single cause of death in the Chicago Lying-in Hospital. Donald (1954) observed 133 cases of respiratory difficulty in newborn infants, of which 57 died. In 26 of these fatal cases, (45.6 per cent), hyaline membrane was found at necropsy - either alone or associated with intraventricular haemorrhage. Undoubtedly the condition must have been present in many cases in the present series.

If the syndrome is fascinating it is because there is as yet no agreement as to the aetiology and treatment, although the clinical picture is a familiar one in a premature baby unit. Bruns and Shields (1954) and Stevenson and Laufe (1955) claimed to have produced hyaline-like membranes in guineapigs - in the one case by the administration of high oxygen concentrations and in the other by tracheal injection of plasma mixed with sediment from amniotic fluid. Potter (1953) maintained that death occurred as a result of congestive pulmonary failure. Lendrum (1955) suggested that the clinical picture "would ordinarily suggest heart failure overloading mainly the pulmonary circuit - failure of the left heart." In this most interesting paper he referred to the sudden increase in effort required by the left heart after birth and/

and suggested that any failure to respond will result in congestion of the pulmonary vessels with possibly a filtration of serum from the capillaries to the alveolar walls and alveolar spaces. He postulated the occurrence of a cycle of increasing pulmonary oedema causing an increasing anoxia of the left ventricle and leading eventually to a complete failure of the over-burdened left heart. Gitlin and Craig (1956) found the membrane to be composed principally of fibrin and postulated that following effusion from the pulmonary circulation, there is conversion of fibrinogen in the effusion to fibrin which then forms the membrane.

These concepts of the disease process are of particular interest since the tendency has been to regard the pulmonary lesions as primary.

Infection

Infection was found in 50 cases at autopsy. Table 37 shows the age at death of these cases and the type of lesion and associated conditions are shown in Table 38. Only 8 per cent of the infections occurred in infants dying during the first 48 hours, which is in direct contrast to the asphyxial group. Figure IX contrasts the age at death for these two main groups.

This alteration in disease processes with length of extra-uterine life is of great interest and is in accordance/

TABLE 37

INFECTION - AGE AT DEATH

Under 24 hours	24-48 hours	3 - 7 days	Over 7 days
3 (6.0)	1 (2.0)	17 (34.0)	29 (58.0)

TABLE 38

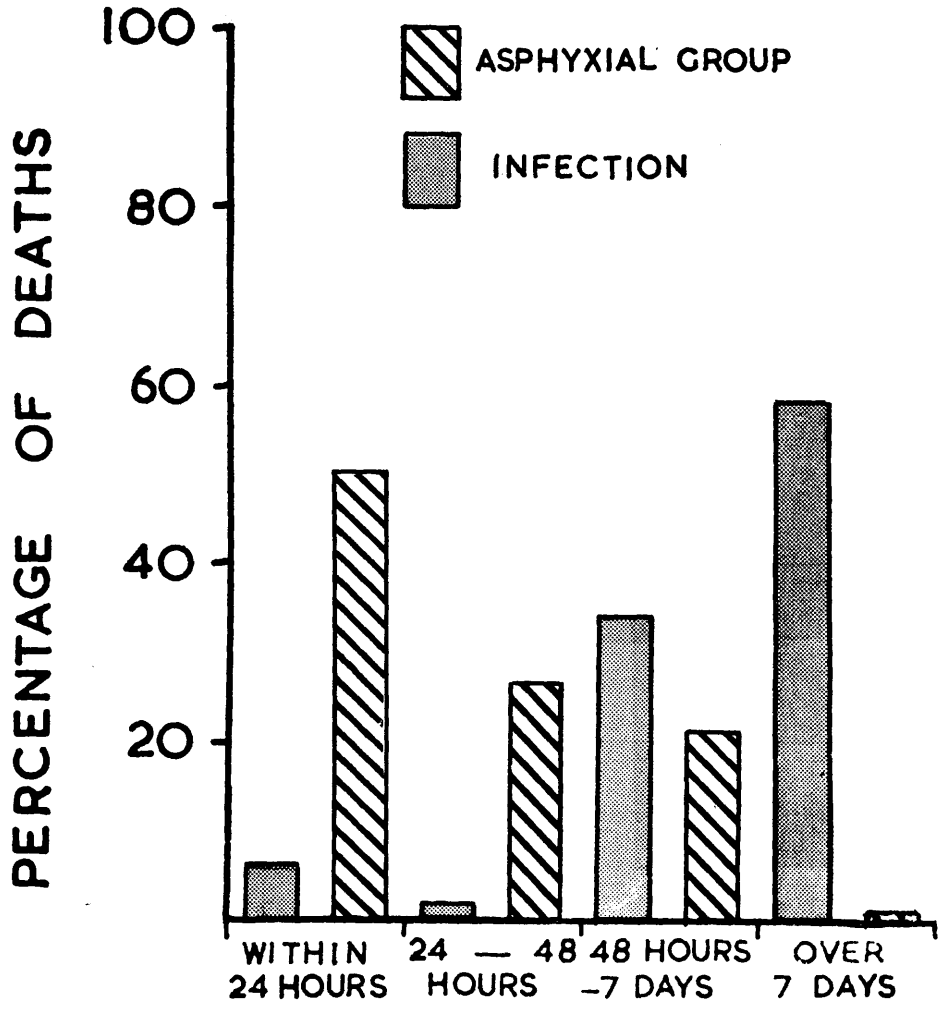
CASES OF INFECTION - TYPE OF LESION

DIAGNOSIS	NO. OF CASES
Broncho-pneumonia	37
Broncho-pneumonia with Erythroblastosis	1
Broncho-pneumonia with Intracranial Haemorrhage	1
Broncho-pneumonia with Intraventricular Haemorrhage	2
Broncho-pneumonia with Kernicterus of Prematurity	4
Broncho-pneumonia with Meningitis	2
Meningitis	1
Meningitis with Pericarditis	1
Septicaemia	1

FIGURE IX

AGE AT DEATH

ASPHYXIAL GROUP AND INFECTION



accordance with the findings in all similar series. Potter (1952) found that when a premature infant dies more than 72 hours after birth, pneumonia is the most frequent cause, the infection in such instances being usually postnatal in origin. Morison (1952) pointed out that while infection is important throughout the whole neonatal period, its importance as a cause of death increases as the "acute disturbances associated with birth are surmounted."

The diagnosis of pneumonia, both during life and at autopsy, frequently presents difficulties. Macgregor (1939) in a study of 541 consecutive neonatal deaths and stillbirths found inflammatory changes in the lungs in 177 cases of which 77 were premature infants. She classified these inflammatory changes into the following four groups:

1. Pneumonias associated with aspiration of contents of the amniotic sac or the vagina.
2. Pneumonias associated with other pulmonary conditions due to stress at birth - these being atelectasis and pulmonary haemorrhage.
3. Postnatal respiratory tract infections -
   a. Bronchopneumonia.
   b. Aspiration pneumonia - aspiration of milk curd or other gastric contents.
   c. Bronchitis.
   d. Terminal hypostatic pneumonia.

4./

4. Haematogenous infection where the involvement of the lungs was secondary to a generalised septicaemia.

She stressed the importance of "neonatal hygiene," since infection contracted after birth must come from the infant's environment and should therefore be preventable. The same author (1948) maintained that many of the cases of pneumonia occurring in the first few days were primarily due to anoxia, the resulting atelectatic lung being a suitable medium for the growth of organisms.

Potter (1952) described the following types of pneumonia in the neonatal period:

1. Intrauterine pneumonia - occurring in stillbirths and in infants dying during the first few days after birth.
2. Bronchopneumonia - in infants more than a few days old.
3. Lipoid pneumonia - following regurgitation and aspiration of milk.
4. Superimposed pneumonia in cases of hyaline membrane.

Both workers stressed the importance of bacteria in the amniotic fluid with consequent aspiration into the foetal lung, and Potter stated that it is surprising that foetal lungs do not become infected more commonly.

Judd (1954) said that in premature labour a broad-spectrum antibiotic should be given to the mother if the membranes/

membranes have been ruptured for more than eight hours or if she has an elevation of temperature - and possibly even in an otherwise uncomplicated long labour.

Newly born infants are particularly susceptible to certain common micro-organisms of relatively low pathogenicity - in particular to the staphylococcus aureus and to coliform bacilli. Even with the most elaborate precautions, minor staphylococcal infections tend to occur in maternity hospitals. (In recent years, an alarming feature of staphylococcal infections in institutions has been the increasing incidence of penicillin-resistent strains, but this was probably of less importance during the years of the survey.) The danger of a minor infection in one infant - or in a mother, nurse, doctor or visitor - is that it may be transmitted and become a fulminating infection in a premature infant. Meningitis is usually associated with a generalised septicaemia. The umbilicus is thought to be the most frequent portal of entry and the infecting organism a coliform bacillus. This condition is well reviewed by Morison (1952).

Epidemic diarrhoea of the new-born is to be dreaded in any institution. There were no deaths attributed to this cause in the survey and fortunately the Paediatric Unit has been free from this infection for many years. This is certainly due to the high standard of nursing

which/

which is maintained - and maintained without the assistance of a central milk kitchen in the hospital.

Macgregor (1955), reviewing two series of neonatal deaths from the Simpson Memorial Pavilion in Edinburgh, found that gastro-enteritis and thrush were not found in the second series which referred to the years 1949 to 1953. She noted the large increase in deaths attributed to "uncomplicated anoxia and hyaline membrane."

Congenital Abnormality

There were 13 neonatal deaths in infants with gross congenital abnormalities. These are detailed in Table 39. Morison (1952) stated that about half of the total foetal and neonatal deaths due to congenital malformations affect the nervous system. In this series the figure is 61.5 per cent for the neonatal deaths.

Rhesus Incompatibility

Five premature infants with erythroblastosis foetalis died during the four-year period. All had replacement transfusions. One died during the transfusion and two shortly afterwards. The fourth and fifth were twins weighing three pounds, one ounce, and three pounds. The first twin died on the sixth day from bronchopneumonia and the second at the age of seven hours, presumably/

TABLE 39

NEONATAL DEATHS - TYPES OF CONGENITAL ABNORMALITIES

DIAGNOSIS	NO. OF CASES
Anencephaly	2
Iniencephaly	1
Hydrocephaly	3
Hydrocephaly, Harelip, Cleft Palate and Absence of Radius and Ulna	1
Klippel-Feil Deformity with Para-oesophageal Hernia	1
Myelo-meningocele	1
Polycystic Kidneys	2
Mongol with Hydronephrosis	1
Harelip and Cleft Palate with "atelectasis")	1

presumably from the co-existing tentorial tear with cerebral haemorrhage.

As previously noted, erythroblastosis in the premature infant is an additional hazard. Replacement transfusions are essential in affected infants to prevent kernicterus but the procedure puts an additional strain on small infants during the period of adaptation to extra-uterine existence.

Kernicterus of Prematurity

There were 4 cases of kernicterus of prematurity, all being associated with bronchopneumonia. It is now recognised that this condition occurs in the absence of rhesus incompatibility in premature infants. (Aidin, Corner and Tovey, 1950, Govan and Scott, 1953) Recently, Allison (1955) has reported the association of kernicterus and haemolytic anaemia with the injection of Vitamin K analogue which he found to produce haemolysis in rats deprived of Vitamin E. Similar findings were noted by Moore and Sharman (1955.) Following this work the report of Laurance (1955) is of particular interest. He related the experience in the Derby Premature Baby Unit where, following on an increase in the routine dosage of "Synkavit," six infants died of kernicterus of prematurity. During the years of the present study "Synkavit" was used routinely in the treatment of the premature infants,

doses/

doses of 5 mgm. being given at birth and occasionally being repeated once. As far as is known, no ill effects were seen. Its use for prophylactic purposes was, however, gradually discontinued during the year 1953. It is now recognised that injections of as little as 1 mgm. will suffice to raise a low prothrombin index to normal.

THE AGE AT DEATH

The age at death has already been discussed for the asphyxial group and for those infants dying from infection. Table 40 shows the age at death for all neonatal deaths according to the autopsy findings and Table 41 shows the age at death according to weight for all the cases. This table shows that 43.7 per cent of the deaths occurred on the first day and a further 20.5 per cent on the second day. In other words, 64.2 per cent - almost two thirds - of the neonatal deaths occurred within forty-eight hours of birth. Greenhill (1947) suggested that the first fifteen minutes after birth is the most dangerous period of life.

Bundesen (1953) reviewed the "natal day" deaths in the City of Chicago and described them as the long-neglected field of infant mortality. Comparing the rates for

TABLE 40

AGE AT DEATH ACCORDING TO AUTOPSY FINDINGS

	Under 24 hrs.	24-48 hours	3 - 7 days	Over 7 days	
Asphyxia	54	30	18	-	102
Intraventricular Haemorrhage	29	15	20	3	67
Other Intracranial Haemorrhage	20	10	7	-	37
Atelectasis	5	-	1	-	6
Infection	3	1	17	29	50
Congenital Abnormality	9	1	-	3	13
Rhesus Incompatibility	4	-	1	-	5
Kernicterus of Prematurity	-	-	3	1	4
Others	1	-	1	-	2
"Prematurity"	9	1	2	-	12
No Autopsy	4	4	6	4	18

TABLE 41

AGE AT DEATH ACCORDING TO WEIGHT

	Under 24 hours	24-48 hours	3 - 7 days	Over 7 days	
Under 2 lb.	32	4	4	-	40
2lb. - 2lb.7oz.	23	13	13	6	55
2½lb. - 2lb.15oz.	20	12	17	11	60
3lb. - 3lb.7oz.	13	8	11	10	42
3½lb. - 3lb.15oz.	13	5	9	5	32
4lb. - 4lb.7oz.	12	10	5	-	27
4½lb. - 4lb.15oz.	10	5	8	2	25
5lb. - 5lb.8oz.	9	5	4	3	21
	132	62	71	37	302

Chicago for the years 1912 and 1952 he showed that during that forty-year period there had been practically no reduction in the mortality on the first day. He ascribed 70 per cent of the early deaths (mature and premature) to "abnormal pulmonary ventilation" and injuries at birth.

Smith and Cook (1955) said that approximately 15 per cent of premature infants die in the neonatal period and usually within the first forty-eight hours. They suggested that the later the death, the more likely is it to be preventable. Dunham (1952) however, studying figures for premature births for the United States of America as a whole, suggested that more infants are now being saved on the first day, only to die in the first week. But Wile (1953) said that, except for those with serious congenital anomalies, premature infants who now survive more than four days will most likely continue to do so. He emphasised the importance of "pediatrically-minded obstetricians and obstetrically-minded pediatricians!"

It is of interest to compare the age at death of the infants in the present series with the similar figures from the hospital for the years 1939 and 1954. Table 42 shows the total premature live births and neonatal deaths for these years with similar figures for the years 1949 to 1952. The age at death is also shown. Although the neonatal mortality rate has been halved, the percentage of the deaths occurring on the first day has almost doubled, whereas the

TABLE 42

COMPARISON OF TOTAL LIVE BIRTHS, NEONATAL DEATHS AND AGE AT DEATH FOR 1939, 1949 - 1952, AND 1954

	TOTAL LIVE BIRTHS	NEONATAL DEATHS				
		TOTAL	UNDER 24 HR.	24 - 48 HOURS	3 - 7 DAYS	OVER 7 DAYS
1939	449	146 (32.5)	58 (39.7)	18 (12.3)	29 (19.9)	41 (28.1)
1949 to 1952	1519	302 (19.9)	132 (43.7)	62 (20.5)	71 (23.5)	37 (12.3)
1954	378	61 (16.1)	42 (68.9)	6 (9.8)	8 (13.1)	5 (8.2)

percentage dying after one week has dropped from 28.1 per cent in 1939 to 8.2 per cent in 1954. Although many factors are concerned, the diminution of morbidity and mortality from infection is undoubtedly the main cause in the latter group. These percentages are shown in graph form in Figure X.

STILLBIRTHS

Of the total of 1,955 premature infants in the series, 436 (22.3 per cent) were stillborn. The total births and stillbirths were shown grouped according to weight in Table 5. Under 3½ pounds the loss is fairly constant for each group, and as the weight then increases, the rate falls accordingly.

The causes of, or factors associated with, stillbirth are many and varied. There may be an inherent defect in the foetus, it may be affected by maternal disease - particularly the toxaemias of pregnancy - or it may be asphyxiated by some interference with its circulation during labour or delivery. In Table 43 the numerous associated factors are reviewed. In several infants two factors co-existed and the case was then included under both headings.

The major groups are the toxaemias of pregnancy, hydramnios and congenital abnormalities.

The/

FIGURE X

NEONATAL MORTALITY RATES AND AGE AT DEATH

1939, 1949 – 1952, 1954.

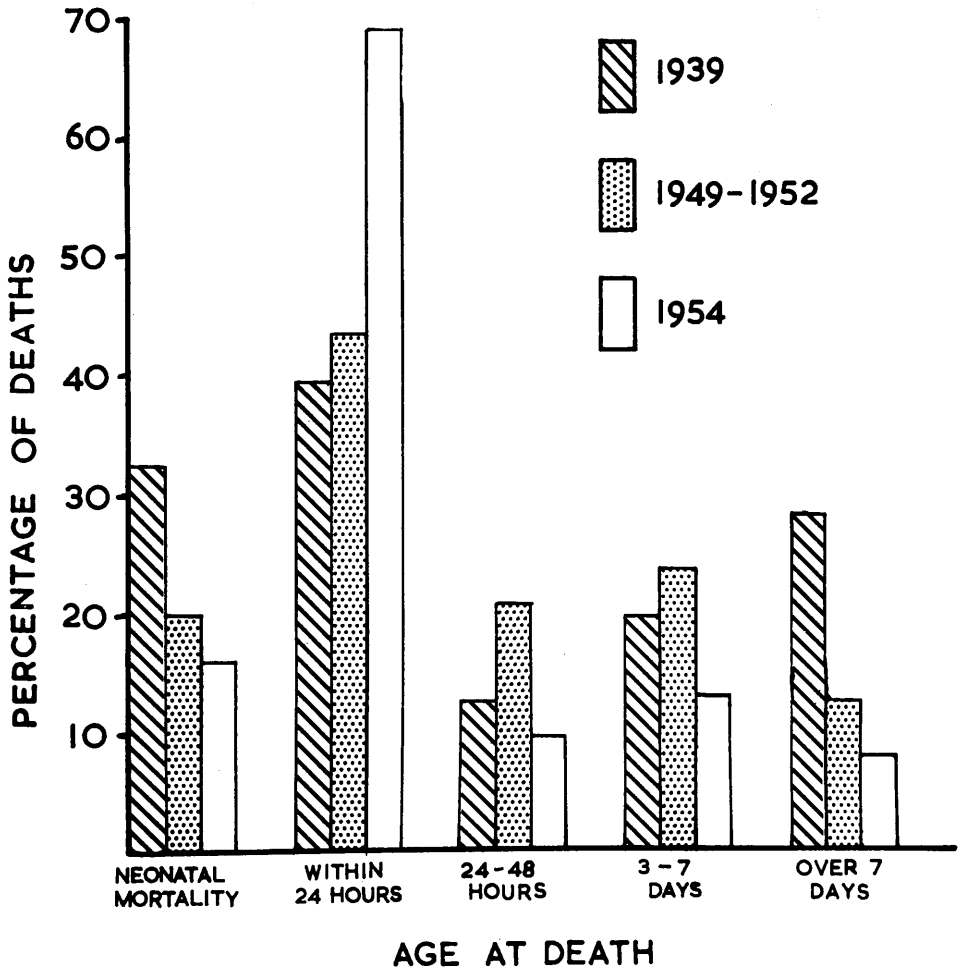


TABLE 43

STILL BIRTHS - ASSOCIATED FACTORS

Toxaemias of Pregnancy	160
Multiple Pregnancy	51
Placenta Praevia	25
Hydramnios	102
Cardiac Disease	8
Rhesus Incompatibility	11
Congenital Abnormalities	116
Prolapsed Cord	12
Velamentous Insertion of Cord	1
True Knot in Cord	3
Cord Round Neck	3
"Asphyxia	9
Tentorial Tear	8
Macerated Foetus - Cause Unknown	8
Intra-Uterine Death Before Labour - Cause Unknown	24

The Toxaemias of Pregnancy

The adverse effects of the toxaemias on the foetus have been discussed in the previous section.

Congenital Abnormalities

In 116 of the stillborn infants (26.6 per cent) there were gross developmental anomalies present. These are classified in Table 44. In 102 cases (87.9 per cent) the abnormality was of the nervous system. This association has been referred to in the section on neonatal deaths. Macgregor (1946) maintained that interest in these abnormalities must be embryological, rather than pathological or clinical.

Hydramnios

In 102 cases of the 436 stillbirths (23.4 per cent) there was an association with hydramnios. This was related to foetal abnormality in 86.6 per cent of cases. Table 45 classifies the cases of hydramnios. In four cases paracentesis had been carried out and in 45 cases the membranes were artificially ruptured. The high incidence of anencephaly has been referred to by Potter (1952.)

Other Groups

In/

TABLE 44

STILL BIRTHS - CLASSIFICATION OF MAJOR CONGENITAL ABNORMALITIES - 116 CASES

ANENCEPHALY - 75 cases

Anencephaly 56
Anencephaly + Meningocele 11
Anencephaly + Meningocele + Exomphalos 4
Anencephaly + Exomphalos 2
Anencephaly + Cleft Palate 2

HYDROCEPHALY - 23 cases

Hydrocephaly 15
Hydrocephaly + Meningocele 6
Hydrocephaly + Multiple Abnormalities 2

ENCEPHALOCELE	1	MULTIPLE DEFORMITIES	1
INIENCEPHALY	3	MONSTER	1
ACHONDROPLASIA	3	RENAL LESIONS	3
EXOMPHALOS	3	Hydronephrosis 1	
MONGOL	2	Polycystic Kidneys 1	
DIAPHRAGMATIC HERNIA	1	Absence of Kidneys 1	

TABLE 45

STILLBIRTHS WITH HYDRAMNIOS - 67 cases

MULTIPLE PREGNANCY - 5 cases

FOETAL ABNORMALITY - 58 cases

Anencephaly	54
Iniencephaly	1
Achondroplasia	2
Hydrocephaly	1

HYDRAMNIOS ALONE - 4 cases

In the majority of the other groups the stillbirths were related to asphyxia. The effect of rhesus incompatibility on the foetus has been discussed previously. In a small proportion of cases (7.3 per cent) there was no apparent cause for the stillbirth, although many of these were very small infants.

GENERAL DISCUSSION

It has been shown that premature birth is one of the major factors concerned in the aetiology of stillbirth and neonatal death. At the Glasgow Royal Maternity and Women's Hospital it is a contributory factor in the perinatal mortality in 59.0 per cent of the cases occurring among all births during the four-year period, 1949 to 1952. If this excessive loss of potential lives is to be reduced, the problems of prematurity must be more clearly understood.

There are three distinct aspects of this problem to be considered:

1. The prevention of premature labour.
2. The management of premature labour once it has become established.
3. The care of the premature infant.

THE PREVENTION OF PREMATURE LABOUR

a. Social and Economic Factors

It has been shown that in 42.3 per cent of the cases in this study, there was no apparent reason for the onset of premature labour or the birth of a premature infant, and it is in this group that social and economic factors play their biggest part. Despite the vast amount

of thought and research that has been devoted to this aspect of the problem, it is clear that no single factor can be incriminated to the exclusion of others. Poor nutrition, over-work, badly-spaced pregnancies, early and late child-bearing, lack of antenatal supervision and sheer ignorance all play their part to a greater or lesser extent. Baird (1953) maintained that we await the attainment of a much higher standard of living before these factors can be discounted. But it must be remembered that higher wages and better housing conditions do not necessarily produce healthier living. Somehow, health education - in its widest sense - must be achieved, but those who know the worst of the city slum-dwellers will agree that any improvement in standards must be very slow. The majority are probably perfectly content with the way of life they have always known - the crowded home, the unskilled job, the unbalanced diet - and will resent any attempt at interference. For many years to come, Social Classes IV and V may be expected to produce a high proportion of premature infants.

b. <u>The Complications of Pregnancy</u>

It is in the management of this group that some progress in prevention can be expected. The fact remains, however, that for complications to be recognised and controlled, the mother must first be under supervision - either/

either by a competent general practitioner or at an efficient antenatal clinic - and such supervision must begin in the early months of pregnancy. Pregnant women, therefore, must be encouraged to seek medical attention. It would seem reasonable to suggest that full payment of maternity benefit grants should depend on regular antenatal supervision. Compulsion in any form is unpopular in this country, but measures must be taken to minimize the damage due to the complications so frequently present in the unsupervised case.

1. The Toxaemias of Pregnancy

It has been pointed out that the incidence of this condition is notoriously high in the West of Scotland, but again much can be done to control the severity of the disease if the mothers are seen and the condition recognised at a sufficiently early stage, as has been shown by Hamlin's work in Sydney (1952.) Prevention of intrauterine death is of great importance in reducing the foetal mortality associated with the toxaemias. Also, with better control, the induction of premature labour or premature termination by Caesarean section should be required much less frequently.

2. Multiple Pregnancy

Russell (1952) and Bender (1952) have been quoted as stressing that adequate rest - preferably in hospital - in the later weeks (or months) of pregnancy will help

to/

to delay the onset of premature labour in multiple pregnancy. However ideal this may be, difficulties are often encountered. The patient may be unable or unwilling to be away from home for so long a period. Often she becomes "bored" in hospital and considers that "nothing is being done" for her. Again, antenatal bed accommodation may not be readily available for these long-term cases. But, should plural pregnancy be associated with increasing hydramnios, then every attempt should be made to have the patient in hospital.

3. Placenta Praevia

Reference has been made to Macafee's contribution to the expectant treatment of ante-partum haemorrhage. Again the patient may become discontented after several weeks in hospital but fear of haemorrhage (if not concern for the fate of her infant) will often suffice to keep her there. There is everything to be gained from the baby's point of view in continuing the pregnancy until it has reached a reasonable size, even if Caesarean section should eventually be required.

4. Cardiac Disease

Again the emphasis must be on adequate antenatal care, with prolonged bed-rest for severe cases. Most authorities are now in agreement that early induction of labour plays no part in the management of these cases. With adequate care and close co-operation with the cardiologist,/

cardiologist, many more pregnancies might proceed to term without causing deterioration in the mother's health. With the recent considerable fall in the incidence of juvenile rheumatism, this problem may not be so acute in the years to come.

5. Hydramnios

The frequent association with foetal abnormality has been shown. Reduction in the incidence of these abnormalities must await a better understanding of their aetiology. Ingalls (1953) reviewing recent work on animal and human experimental embryology stated that "it is much too soon in the 1950's to present an over-all program directed towards preventing congenital malformations. Far too little is known epidemiologically about human defects."

However, in the individual case, if X-ray shows no evidence of foetal abnormality there is everything to be gained from ensuring adequate rest in the hope of preventing the onset of premature labour. As has been mentioned, this is particularly important when the hydramnios is associated with multiple pregnancy.

6. The Miscellaneous Group

Prompt treatment of acute febrile illnesses during pregnancy may prevent the onset of labour, particularly if the temperature can be controlled quickly. Induction

of/

of labour in cases of rhesus incompatibility has been discussed and shown to be inadvisable, except in a few selected cases. However, until a new method of approach to this problem is found, early intra-uterine deaths will still occur in severely sensitised patients.

With regard to diabetes mellitus, rigid control is necessary throughout pregnancy. Although induction of labour - or termination of the pregnancy by Caesarean section - is frequently the treatment of choice, this is generally not undertaken until the 36th week of gestation by which time the majority of these infants have "outgrown" the range of prematurity.

To summarise, prevention of prematurity depends on a healthier mode of living for the lower social classes and on early and adequate antenatal supervision, with prompt treatment of all complications and hospital admission where necessary. On both accounts, however, it is obvious that the public must co-operate. In the first place, the onus is on the pregnant woman to seek advice. Secondly, the advice given must be taken - the prescription for iron is useless unless the patient takes the medicine, and there is no point in providing additional antenatal beds if the women will not come into hospital.

THE MANAGEMENT OF PREMATURE LABOUR

It should be mentioned at this point that the patient who threatens to go into labour prematurely may occasionally settle with treatment by bed-rest and the use of adequate sedation, generally with morphine. She may then be able to continue her pregnancy for a few more days or weeks. Obviously, it is only at the very commencement of labour that sedation can succeed, and not infrequently the question as to whether or not there is still time to try and suppress contractions is a very difficult one. Particularly in parous women, morphine if used too late to stop the contractions, may seriously affect the infant born a few hours later. With the primigravid patient, the duration of labour is generally considerably longer and the sedative will have had time to lose its maximum effect before the birth of the infant.

Mention should be made, too, of the patient with prematurely ruptured membranes. These women should be admitted to hospital for bed-rest in the hope of delaying the onset of labour. There is of course a very real danger of intra-uterine infection occurring and it is now considered that a broad-sprectrum antibiotic should be given. There is as yet no agreement as to the drug of choice but it must be remembered that in hospital the main hazard to the infant will be from coliforms and penicillin-resistent strains/

strains of staphylococci.

Once premature labour is established, several factors should be borne in mind. As already discussed, sedation should be MINIMAL. If analgesia is necessary, gas- and-oxygen is probably the least harmful to the foetus and it is now appreciated that oxygen administered between contractions is of real value. Eastman (1954), in a stimulating address entitled "Mount Everest in Utero" drew attention forcibly to the low oxygen environment to which the foetus is adapted. Again, if general anaesthesia is required, oxygenation must be as generous as possible. More use might be made of local and spinal techniquesfor forceps and section deliveries.

As regards the actual delivery, much is to be gained from early and adequate episiotomies, both in vertex and breech deliveries, and the prompt and skilled application of forceps to the after-coming head in breech deliveries is of real value. Too often the actual delivery of the small premature infant is regarded as unimportant by the obstetricians, yet more skill may be required in dealing with a "breech" weighing 3 pounds than in one weighing 6 pounds.

In brief, the management of premature labour must be directed towards the prevention of anoxia in the infant about to be born.

THE CARE OF THE PREMATURE INFANT

This must start at birth, and again the all-important factor is the prevention and treatment of anoxia. The extreme importance of anoxia or asphyxia as a cause of neonatal death in premature infants has been demonstrated, but it must not be forgotten that the lessening of the incidence of infection is certainly due to the constant vigilance of the nursing staff and to the strict precautions for its prevention that are taken in the Paediatric Unit, and not to any change in the virulence of organisms. Such vigilance must, of course, be fully maintained.

It is beyond the scope of this thesis to discuss in detail the care of the newly-born premature infant. There has, indeed, been much progress made in this field since the years covered by this study. It should be mentioned, however, that an incubator was available in the Paediatric Unit during only the last five months of the period reviewed. At that time, too, intragastric oxygen was not used, nor were any mechanical forms of resuscitation.

It is hoped that with a growing appreciation of the effects of anoxia, more will be done to prevent its occurrence. Prevention must always be better than any attempt at treatment can be. Indeed, unlimited use of oxygen in the care of premature infants can no longer be permitted./

permitted. The association with retrolental fibroplasia has already been referred to and it has been suggested that high concentrations of oxygen may be associated with the formation of hyaline membrane. (Bruns and Shields, 1954). A recent annotation in the British Medical Journal (1955) stresses the fact that high concentrations can no longer be regarded as harmless to human infants. Far better, then, that the premature infant should be born in a healthy state, well prepared to fight for his life - as indeed he will if his vital centres are not paralysed by anoxia.

Much stress has been laid on the causes and prevention of premature labour and on the foetal mortality associated with it. It might be thought that great improvements are possible in the near future - but this is doubtful. Many cases of premature labour undoubtedly are preventable, but the problems pertaining to Social Classes IV and V will be with us for many years to come. Also, as Brooks (1952) and his colleagues pointed out, with better antenatal and obstetric care fewer miscarriages should occur - but some of thes pregnancies may well result in the birth of small premature infants. Similarly, the birth of larger prematures may be delayed until in fact the babies are outwith the premature weight group. They suggested that the mortality rates may even increase due to the relatively greater number of smaller infants. It should be/

be borne in mind, too, from the statistical point of view that at a gestation period of 26 or 27 weeks, the dead-born foetus is classified as a miscarriage, but, if it be born alive, it is regarded (and rightly so) as a premature live birth - and will almost certainly require to be classified as a neonatal death also.

Thus the importance of the management of premature labour and the after-care of the premature infant cannot be too highly stressed. Progress will depend on full co-operation between Wile's "pediatrically-minded obstetricians and obstetrically-minded pediatricians."

SUMMARY AND CONCLUSIONS

There is an excessive perinatal mortality associated with prematurity which is reflected in the national stillbirth and neonatal death rates.

In an attempt to clarify some of the problems related to prematurity, an analysis has been made of the 1,955 premature infants born in the Glasgow Royal Maternity and Women's Hospital during the four-year period, 1949 to 1952.

It has been shown that the perinatal mortality rate for this series of infants was 37.7 per cent. When the infants were grouped according to weight, the numbers in each group and the chance of survival were greater with increasing weight.

In 42.3 per cent of the cases studied, there was no apparent cause for the onset of premature labour. The effect of social and economic factors on this group has been discussed. The commonest complications of pregnancy associated with the birth of premature infants were found to be the toxaemias of pregnancy and multiple pregnancy.

The necessity of prevention of anoxia during labour and at delivery has been discussed. It has been shown that particular care is required with breech deliveries.

The importance of asphyxia as a cause of death has been demonstrated. The high percentage of deaths occurring/

occurring within 48 hours of birth is evidence of this. Also, the importance of the prevention of infection should always be borne in mind.

It is suggested that there are three distinct aspects to the problem of prematurity:

1. The prevention of premature labour.
2. The management of premature labour, particularly with a view to the prevention of anoxia.
3. The care of the premature infant.

Of these aspects the most important obviously is prevention and there is therefore an urgent need for much more information on the aetiology of premature birth.

BIBLIOGRAPHY

AARON, J.B. and HALPERIN, J.

(1955) Fetal survival in 376 twin deliveries. Amer. J. Obstet. Gynec., 69 794.

AIDIN, R., CORNER, B. and TOVEY, G.

(1950) Kernicterus and prematurity. Lancet, I, 1153.

ALLISON, A.C.

(1955) Danger of vitamin K to newborn. Lancet, I, 669.

ANNOTATION

(1955) Pulmonary hyaline membrane. Brit. med. J., 2, 1611.

ASHBY, H.T.

(1915) Infant Mortality. Cambridge University Press.

ASHTON, N., WARD, B. and SERPELL, G.

(1953) Role of oxygen in the genesis of retrolental fibroplasia. Brit. J. Ophthal., 37, 513.

BAIN, K., HUBBARD, J.P. and PENNELL, M.Y.

(1949) Hospital fatality rates for premature infants. Pediatrics, 4, 454.

BAIRD, D.

(1945) The influence of social and economic factors on stillbirths and neonatal deaths. J. Obstet. Gynaec. Brit. Emp., 52, 217.

BAIRD, D.

(1947) Social class and foetal mortality. Lancet, II, 531.

BAIRD, D., THOMSON, A.M. and DUNCAN, E.H.L.

(1953) The causes and prevention of stillbirths and first week deaths. Part II : Evidence from Aberdeen clinical records. J. Obstet. Gynaec. Brit. Emp., 60, 17.

BAIRD, D., WALKER, J. and THOMSON, A.M.

(1954) The causes and prevention of stillbirths and first week deaths. Part III: A classification of deaths by clinical cause: the effect of age, parity and length of gestation on death rates by cause. J. Obstet. Gynaec. Brit. Emp., 61, 433.

BARRY, A.P.

(1952) The obstetrical management of the cardiac patient. Irish J. med. Sci., 6th series, 398.

BECK, A.C.

(1941) How can the obstetrician aid in reducing the mortality of prematurely born infants? Amer. J. Obstet. Gynec., 42, 355

BECK, A.C.

(1946) The obstetrician's responsibility for the hazards of the first few days of life with special reference to anoxia and prematurity. Amer. J. Obstet. Gynec., 51, 173

BENDER, S.

(1952) Twin pregnancy. A review of 472 cases. J. Obstet. Gynaec. Brit. Emp., 59, 510

BOURNE, A.W. and WILLIAMS, L.H.

(1948) Recent Advances in Obstetrics and Gynaecology. 7th Ed. J.&A. Churchill, London.

BRASH, A.A.

(1949) The effect of toxaemia of pregnancy upon the foetus and newborn child. Arch. Dis. Childh., 24, 107

BROCKWAY, G.E., REILLY, E.T. and RICE, M.M.

(1950) Premature Mortality.
J. Pediat., 37, 362.

BROOKS, M.B., CASS, A.B. and CHINNOCK, R.F.

(1952) Premature infant mortality.
Amer. J. Dis. Child., 83, 642.

BROWNE, F.J.

(1950) Postgraduate Obstetrics and Gynaecology.
Butterworth, London.

BROWNE, F.J.

(1955) Antenatal and Postnatal Care.
8th Ed. (with McClure Browne, J.C.)
J. & A. Churchill, London.

BRUNS, P.D. and SHIELDS, L.V.

(1954) High oxygen and hyaline-like membranes.
Amer. J. Obstet. Gynec., 67, 1224.

BUNDESEN, H.N.

(1953) Natal day deaths. The long-neglected field of infant mortality.
J. Amer. med. Ass., 153, 466.

CAMERON, C.S. and GRAHAM, S.

(1944) Antenatal diet and its influence on stillbirths and prematurity.
Glasg. med. J., 24, 1.

CAREY, H.M.

(1955) Toxaemias of Pregnancy in Donald's Practical Obstetric Problems.
Lloyd-Luke, London.

CLAIREAUX, A.E.

(1953) Hyaline membrane in the neonatal lung.
Lancet, II, 749.

CLIFFORD, S.H.

(1953) Role of the pediatrician in prevention of needless neonatal deaths.
J. Amer. med. Ass., 153, 473.

CLIFFORD, S.H.

(1955) The problem of prematurity. Obstetric, pediatric and socioeconomic factors.
J. Pediat., 47, 13.

COLE, W. C.C. (1954) in Care of the Premature Infant. Pediatric Clinics of North America. Saunders, Philadelphia and London.

COLEMAN, D.J. and DAY, B.L. (1956) Anaesthesia for operative obstetrics. Value of cuffed endotracheal tube. Lancet, I, 708

COMBE, A. (1840) A Treatise on the Physiological and Moral Management of Infancy. Maclachlan & Stewart, Edinburgh.

CRAWFORD, J.S. (1956) Some aspects of obstetric anaesthesia. Brit. J. Anaesth., 28, 146

CROSSE, V.M. (1952) The Premature Baby. 3rd Ed. J. & A. Churchill, London.

CROSSE, V.M. (1954) Prematurity in Recent Advances in Paediatrics. J. & A. Churchill, London.

CROSSE, V.M. and MACKINTOSH, J.M. (1954) Perinatal Mortality in Recent Advances in Paediatrics. J. & A. Churchill, London.

DALY, C., HEADY, J.A. and MORRIS, J.N. (1955) Social and biological factors in infant mortality. III. The effect of mother's age and parity on social-class differences in infant mortality. Lancet., I, 445

DAVIES, B.S., GERRARD, J. and WATERHOUSE, J.A.H. (1953) The pattern of haemolytic disease of the newborn. Arch. Dis. Childh., 28, 466

DEPARTMENT OF HEALTH FOR SCOTLAND. (1943) Infant Mortality in Scotland. H.M.S.O., Edinburgh.

DIAMOND, L.K. (1947) Erythroblastosis foetalis or haemolytic disease of the newborn. Proc. Roy. Soc. Med., 40, 546

DIDDLE, A.W. and PLASS, E.D. (1942) Mortality of prematurely born infants. Amer. J. Obstet. Gynec., 44, 279

DONALD, I. (1954) Atelectasis neonatorum. J. Obstet. Gynaec. Brit. Emp., 61, 725

DONALD, I. (1955) Practical Obstetric Problems. Lloyd-Luke, London.

DOUGLAS, J.W.B. (1950) Some factors associated with prematurity. The results of a national survey. J. Obstet. Gynaec. Brit. Emp., 57, 143

DOUGLAS, C.A. and McKINLAY, P.L. (1953) The incidence of prematurity in Scotland and its importance in early infant mortality. Hlth. Bull. (Edinb.,) 11, 4

DRILLIEN, C.M. (1947) Studies in prematurity, stillbirth and neonatal death. Part I. Factors affecting birth weight and outcome. J. Obstet. Gynaec. Brit. Emp., 54, 300

DRILLIEN, C.M. (1947) Studies in prematurity, stillbirth and neonatal death. Part II. Delivery and its hazards. J. Obstet. Gynaec. Brit. Emp., 54, 443

DUNCAN, E.H.L., BAIRD, D. and THOMSON, A.M. (1952) The causes and prevention of stillbirths and first-week deaths. Part I. The evidence of vital statistics. J. Obstet. Gynaec. Brit. Emp., 59, 183

DUNHAM, E.C. (1952) Factors associated with reduction of premature infant mortality rates in the United States. J. Pediat., 41, 697

EASTMAN, N.J. (1951) Causes and management of premature birth. (Annotation) Lancet, II, 723

EASTMAN, N.J. (1954) Mount Everest in utero. Amer. J. Obstet. Gynec., 67, 701

EBBS, J.H., TISDALL, F.F. and SCOTT, W.A. (1941) The influence of prenatal diet on the mother and child. J. Nutrit., 22, 515

EDITORIAL. (1905) Practitioner, 75, 583

EDITORIAL. (1956) Thiopentone (?) in obstetrics. Brit. J. Anaesth., 28, 145

FERGUSON, T. (1948) The Dawn of Scottish Social Welfare. Nelson, Edinburgh.

FERGUSON, A.E., BROWN, A.C. and FERGUSON, T. (1952) Some circumstances affecting the survival of premature children. Glasg. med. J., 33, 143

FRANKLIN, A.W. (1953) Mortality in prematurity. Discussion on some problems of prematurity. Proc. Roy. Soc. Med., 46, 877

GITLIN, D. and CRAIG, J.M. (1956) The nature of the hyaline membrane in asphyxia of the newborn. Pediatrics, 17, 64

GLASGOW ROYAL MATERNITY AND WOMEN'S HOSPITAL. Medical Report for the Year 1952 Aird & Coghill, Glasgow.

GOVAN, A.D.T. and SCOTT, J.M. (1953) Kernicterus and prematurity. Lancet, I, 611.

GRAHAM, S. (1935) Prematurity and neonatal mortality. Arch. Dis. Childh., 10, 210.

GREENHILL, J.P. (1947) Foetal and neonatal mortality. J. Obstet. Gynaec. Brit. Emp., 54, 577

HAMLIN, R.H.J. (1952) The prevention of eclampsia and pre-eclampsia. Lancet, I, 64

HEADY, J.A., DALY, C. and MORRIS, J.N.

(1955) Social and biological factors in infant mortality. II. Variation of mortality with mother's age and parity. Lancet, I, 395

HEADY, J.A., STEVENS, C.F., DALY, C. and MORRIS, J.N.

(1955) Social and biological factors in infant mortality. IV. The independent effects of social class, region, the mother's age and her parity. Lancet, I, 499

HELLMAN, L.M.

(1953) in Prematurity, Congenital Malformation and Birth Injury. Association for the Aid of Crippled Children, New York.

HENDERSON, J.L.

(1946) The statistics of prematurity. A plea for standardisation. Arch. Dis. Childh., 21, 105

HESS, J.H.

(1923) Premature and Congenitally Diseased Infants. J. & A. Churchill, London.

HSIA, D.Y., ALLEN, F.H. jun., DIAMOND, L.K. and GELLIS, S.S.

(1952) Erythroblastosis fetalis: serum bilirubin. Amer. J. Dis. Child., 84, 640

HUGGETT, A. St.G.

(1946) Some applications of prenatal nutrition to infant development. Brit. med. Bull., 4, 196

IELSLEY, R.

(1955) Social class selection and class difference in relation to stillbirths and infant deaths. Brit. med. J., 2, 1520

INGALLS, T.H.

(1953) Preventive Prenatal Pediatrics in Advances in Pediatrics. Volume VI. Interscience Publishers, London.

JUDD, G.E.

(1954) Management of labor in reference to prevention of perinatal mortality. J. Amer. med. Ass., 156, 1474

LAURANCE, B.

(1955) Danger of vitamin - K analogues to newborn. Lancet, I, 819

LEADING ARTICLE.

(1954) Policy for "prematures." Lancet, I, 29

LENDRUM, F.C.

(1955) The "pulmonary hyaline membrane" as a manifestation of heart failure in the newborn infant. J. Pediat., 47, 149

MACAFEE, C.H.G.

(1945) Placenta praevia - a study of 174 cases. J. Obstet. Gynaec. Brit. Emp., 52, 313

MACAFEE, C.H.G.

(1950) Hydramnios. J. Obstet. Gynaec. Brit. Emp., 57, 171

MASTERS, W.H. and ROSS, R.W.

(1949) Conduction anaesthesia. Protection afforded the premature infant. J. Amer. med. Ass., 141, 909

MINSTRY OF HEALTH.

(1949) Neonatal Mortality and Morbidity. H.M.S.O., London.

MOLLISON, P.L., MOURANT, A.E. and RACE, R.R.

(1952) The Rh. Blood Groups and their Clinical Effects. H.M.S.O., London.

MOLLISON, P.L. and WALKER, W.

(1952) Controlled trials of the treatment of haemolytic disease of the newborn. Lancet, I, 429

MOORE, T. and SHARMAN, I.M.

(1955) Danger of vitamin -K analogues to newborn. Lancet, I, 819

MORISON, J.E.

(1952) Foetal and Neonatal Pathology. Butterworth, London.

MORRIS, J.N. and HEADY, J.A.

(1955) Social and biological factors in infant mortality. I. Objects and methods. Lancet, I, 343

MURDOCH, D. and FOULKES, J.F.

(1952) Antepartum haemorrhage. J. Obstet. Gynaec. Brit. Emp., 59, 786

MACGREGOR, A.R.

(1939) Pneumonia in the newborn. Arch. Dis. Childh., 14, 323

MACGREGOR, A.R.

(1946) The pathology of still-birth and neonatal death. Brit. med. Bull., 4, 174

MACGREGOR, A.R.

(1948) Neonatal Mortality and Morbidity. B.M.A. Proceedings of the Annual Meeting 1948. Butterworth, London.

MACGREGOR, A.R.

(1955) The incidence of infection in neonatal deaths. Arch. Dis. Childh., 30, 299

NIXON, W.C.W.

(1953) The prevention of prematurity. Discussion on some problems of prematurity. Proc. Roy. Soc. Med., 46, 877

PECKHAM, C.H.

(1938) Statistical studies on prematurity. J. Pediat., 13, 474

POTTER, E.L. and ADAIR, F.L.

(1939) Factors associated with fetal and neonatal deaths. J. Amer. med. Ass., 112, 1549

POTTER, E.L.

(1952) Pathology of the Fetus and the Newborn. Year Book Publishers, Chicago.

POTTER, E.L.

(1953) Pulmonary Pathology in the Newborn in Advances in Pediatrics. Volume VI. Interscience Publishers, London.

POTTER, E.L.

(1954) The trend of changes in causes of perinatal mortality. J. Amer. med. Ass., 156, 1471

REGISTRAR-GENERAL FOR SCOTLAND.

(1955) Hundredth Annual Report, 1954. H.M.S.O., Edinburgh.

ROYAL COLLEGE OF OBSTETRICIANS AND GYNAECOLOGISTS AND THE POPULATION INVESTIGATION COMMITTEE.

(1948) Maternity in Great Britain. Oxford University Press, London.

RUSSELL, G.R. and BETTS, W.A.

(1952) Natal and neonatal factors in premature infant mortality. J. Pediat., 40, 722

RUSSELL, J.K.

(1952) Maternal and foetal hazards associated with twin pregnancy. J. Obstet. Gynaec. Brit. Emp., 59, 208

SANDIFER, S.C.

(1944) Premature birth. (Analysis of 1,000 cases) Incidence, aetiology and immediate result to the baby. J. Obstet. Gynaec. Brit. Emp., 51, 408

SMITH, C.A.

(1951) The Physiology of the Newborn Infant. 2nd Ed. Blackwell Scientific Publications, Oxford.

SMITH, C.A. and COOK, C.D.

(1955) Special problems of the newborn. Summary of round table discussion. Pediatrics, 15, 348

STEVENSON, S.S. and LAUFE, L.E.

(1955) Experimental production of the pulmonary hyaline membrane syndrome. J. Pediat., 47, 40.

TAYLOR, E.S., PHALEN, J.R. and DYER, H.L.
(1949) Effect of obstetric difficulties and maternal disease on premature infant mortality.
J. Amer. med. Ass., 141, 904

TAYLOR, E.S., SCOTT, W.C. and GOVAN, C.D.
(1951) Studies of blood oxygen saturation and causes of death in premature infants.
Amer. J. Obstet. Gynec., 62, 764

TAYLOR, E.S.
(1954) in Care of the Premature Infant.
Pediatric Clinics of North America.
Saunders, Philadelphia and London.

TITMUSS, R.M.
(1943) Birth, Poverty and Wealth.
Hamish Hamilton, London.

TYSON, R.M.
(1946) A fifteen-year study of prematurity.
J. Pediat., 28, 648.

UNITED NATIONS.
(1954) Foetal, Infant and Early Childhood Mortality. Volume I. The Statistics.
United Nations, New York.

WALKER, W. and NELIGAN, G.A.
(1955) Exchange transfusion in haemolytic disease of the newborn.
Brit. med. J., I, 681

WALKER, W. and MURRAY, S.
(1956) Haemolytic disease of the newborn as a family problem.
Brit. med. J., I, 187

WALLACE, H.M.
(1953) in Prematurity, Congenital Malformation and Birth Injury.
Association for the Aid of Crippled Children, New York.

WALLACE, H.M., GOLD, E.M., BAUMGARTNER, L., LOSTY, M.A. and RICH, H.
(1954) Trends in maternal and perinatal mortality in New York City.
J. Amer. med. Ass., 155, 716

WILE, S.A. (1953) Progress in the reduction of neonatal mortality. Amer. J. Obstet. Gynec., 66, 131

WOOLF, B. (1946) Vital statistics of stillbirths and neonatal deaths. Brit. med. Bull., 4, 170.