have been normal and no cerebral signs had been seen; but we cannot, of course, be sure that he did not suffer perinatal cerebral damage.

The prognosis, therefore, appears to be very good for babies who survive the initial episode of chilling. Only 3 out of 36 had disabilities which might possibly be attributable to it—namely, cerebral palsy, mild mental retardation, and epilepsy with mild mental retardation. With one exception there was no interference with growth and physical or mental development in the remainder.

Discussion

Cold injury is, for the most part, a preventable disease. If ever central heating becomes a widespread method of heating houses in this country, then its incidence will presumably decrease. Apparently it is almost unknown in North America, probably because there the houses are properly warmed and many more confinements take place in hospital. However, it seems unlikely that many bedrooms in Britain will be efficiently warmed for some time to come, and therefore active measures will be needed to prevent the condition. The most important measure is the education of all who handle newborn babies at home in the danger of its occurrence during the cold months of the year, in the factors which predispose to it, and in its recognition. The appendix to the paper of Mann and Elliott (1957) sets out simple rules for midwives which, if followed, would substantially reduce the incidence of this disease. The recognition that a baby is chilled is also important, and in the early stages this can be difficult unless the condition is kept in mind. The complaint by the parent or midwife that a baby in the first week of life is refusing to feed, that it is cold, or that the limbs are swollen is highly significant in the cold months of the year. Unfortunately a low-reading thermometer will seldom be carried by the practitioner or midwife.

Probably all chilled babies should be admitted to hospital. Certainly the severely chilled ones need all the resources of modern paediatric care, even though the details of treatment are still controversial.

Summary

All hypothermic newborn babies (183) admitted to the Children's Hospital, Birmingham, over an 11-year period were classified into aetiological groups. Seventy of these were examples of "primary cold injury," the most important or only factor being external chilling.

In three-quarters of the 70 babies the minimum air temperature at the start of their illness was below 35° F. (1.7° C.); in four-fifths the chilling occurred in January to March. Other factors thought to be important are delay in wrapping the baby after birth, tight wrapping, failure to heat the room at night, as well as factors inherent in the neonate. Nearly all were born at home.

The commonest *symptoms* were feeding difficulty, oedema, coldness to touch, and lethargy. Symptoms dated from birth in a third and from the first week in four-fifths. The commonest *signs* on admission were oedema (77%), immobility, a florid complexion, and sclerema. Oedema is thus an important pointer to the diagnosis.

Oliguria was common in severe cases, and in a small investigation the blood urea, phosphorus, and potassium were found to be elevated.

Treatment varied, but it is agreed that warming should be slow.

One-quarter of the babies died. Pulmonary haemorrhage was a universal finding at necropsy.

A follow-up survey of 36 (69%) survivors showed that 92% were normal. One child has cerebral palsy and two are mentally retarded to a mild degree.

We thank the consultant staff of the Children's Hospital for access to their patients; Professor J. M. Smellie for his advice and encouragement; Dr. H. Baar for necropsy reports; Professor D. V. Hubble and Dr. O. H. Wolff for helpful criticism; successive residents for careful case-notes; the nursing staff for their observations and nursing care; and the director of the Edgbaston Meteorological Observatory for climatic information.

REFERENCES

Bower, B. D. (1954). *Quart. J. Med.*, **23**, 215.
—— (1956). M.D. thesis, University of Birmingham.
Braithwaite, J. V. (1955). *Lancet*, **1**, 773.
Farquhar, J. W. (1957). Ibid., **1**, 371.
Henoch, E. (1889). *Lectures on Children's Diseases*, translated by John Thomson, Vol. 1. New Sydenham Society, London.
Herlitz, G. (1943). *Acta paediat. (Stockh.)*, **30**, 434.
Jones, H. E. (1955). *Lancet*, **1**, 679.
Mann, T. P. (1955). Ibid., **1**, 613.
—— (1958). *Brit. med. J.*, **2**, 228.
—— and Elliott, R. I. K. (1957). *Lancet*, **1**, 229.
Oppé, T. E., and Simpson, K. (1957). Ibid., **1**, 327.
Polani, P. E. (1955). Ibid., **1**, 773.
—— (1958). Height and Weight Charts, Medical Research Unit, National Spastics Society, Guy's Hospital, London.
Smallpeice, V. (1955). *Lancet*, **1**, 679.
Williamson, D. A. J. (1955). Ibid., **1**, 773.

ANENCEPHALY AND OTHER CONGENITAL ABNORMALITIES

AN EPIDEMIOLOGICAL STUDY IN NORTHAMPTONSHIRE

BY

M. J. PLEYDELL, M.C., M.D., D.P.H.

County Medical Officer of Health, Oxfordshire; Lately Deputy County Medical Officer of Health, Northamptonshire

Congenital abnormalities merit the same detailed epidemiological study to-day which in the past has been devoted to infectious disease. The necessary information can be obtained from the local authority and hospital records; medical practitioners and health visitors can give invaluable help in providing details of individual cases. In Northamptonshire a register of congenital abnormalities has been compiled for each local authority district from 1944. The information has been obtained as follows:

1. Routine searches have been made of the hospital birth registers, the domiciliary birth registers, and the infant mortality registers.

2. All midwives and health visitors have been asked to notify congenital abnormalities. Recently a new section has been added to the midwives' antenatal records and the health visitors' infant record cards asking for a definite statement whether or not an abnormality is present.

3. With the co-operation of the consultant obstetricians and paediatricians, their records have been made available for scrutiny in those cases where a congenital abnormality is present.

4. The records of the mental health department have been examined in regard to mental defectives; the records of the handicapped pupils register of the school health department have also been examined for children with congenital defects.

5. The health visitors and midwives of the local health authority have been asked to ascertain the address or addresses at which the mothers were living throughout pregnancy.

6. In nearly every case it has been possible to confirm the diagnosis by medical opinion.

From these sources the following information is presented.

Anencephaly

Incidence

The great majority of case records of anencephaly and other abnormalities of the central nervous system have been obtained from the hospital birth registers. The incidence of these and other abnormalities is shown in Table I. It will be seen that the figures for Northamptonshire are comparable with those obtained by Penrose (1955) from Queen Charlotte's Hospital and University College Hospital.

TABLE I.—*Births of Infants with Congenital Abnormalities in Northamptonshire, 1944–57*

Year	No. of Live and Still-births	No. of Cases of					
		Mongolism	Congenital Heart Disease	Hare-lip; Cleft-palate	Anencephaly	Spina Bifida	Hydrocephaly
1944	4,798	6	16	10	3	10	1
1945	4,443	7	10	4	2	7	3
1946	4,639	4	10	7	4	9	1
1947	5,011	8	18	1	6	10	3
1948	4,423	5	13	11	1	5	2
1949	4,127	7	18	5	2	5	1
1950	4,078	6	17	12	7	6	2
1951	4,096	9	12	5	3	7	4
1952	4,090	6	13	6	6	16	—
1953	4,342	12	11	4	7	6	2
1954	4,396	9	14	8	7	8	4
1955	4,286	7	10	11	3	12	6
1956	4,656	10	7	12	6	10	7
1957	4,839	3	26	5	7	5	2
Total	62,224	99	195	101	64	116	38
Incidence % live and still-births		0·16	0·31	0·16	0·1	0·19	0·06
Incidence % in University College Hospital and Queen Charlotte's Hospital (1947–51) (Penrose) ..		0·2	0·24	0·11	0·15	0·125	0·09

Geographical Distribution of Births

When the births of abnormalities of the central nervous system are plotted out on the map it becomes evident that they are more common in urban than in rural areas. In particular, the urban incidence of anencephaly and hydrocephaly is about double the rural incidence (Table II). Most cases in rural areas are born not far distant from towns. Thus in 1956 and 1957 only 3 of the 13 patients with anencephaly were born in local authority rural districts, and one of these was, in fact, born on a housing estate on the Northampton borough boundary.

If the distribution of anencephaly is studied in more detail it will be found that the highest incidence of cases occurs in the industrial belt. From a geographical aspect Northamptonshire is primarily a a rural county; but an industrial belt associated with ironstone extraction, steel manufacture, boot and shoe production, clothing, and light engineering traverses its northern waist (Fig. 1). Although the ratio of live births and stillbirths in the industrial belt in proportion to the rest of the county is only 1.3 : 1, a similar ratio of anencephalic births is 4 : 1. Anencephaly, therefore, is three times as common in the industrial belt as elsewhere in the county.

TABLE II.—*Urban and Rural Incidence of Congenital Abnormalities and some Notifiable Diseases in Northamptonshire* (1944–57)

	Total	Boroughs and Local Authority Urban Districts	Local Authority Rural Districts	Ratio Urban: Rural
Live births	60,890	32,484	28,406	1·1 : 1
Abnormalities:				
Anencephaly (including anencephaly with spina bifida) ..	64	43 (40)	21 (18)	2·0 : 1
Hydrocephaly ..	38	25 (21)	13 (13)	1·9 : 1
Spina bifida (including spina bifida with hydrocephaly) ..	116	67 (54)	49 (47)	1·4 : 1
Congenital heart disease	195	92 (86)	103 (99)	0·9 : 1
Cleft-palate/hare-lip	101	57 (51)	44 (41)	1·3 : 1
Mongolism	99	49 (49)	50 (50)	1·0 : 1
Notifiable infections:				
Scarlet fever	4,515	2,569	1,946	1·3 : 1
Whooping-cough ..	7,997	3,775	4,222	0·9 : 1
Poliomyelitis	380	226	154	1·5 : 1
Measles	35,342	20,739	14,603	1·4 : 1
Erysipelas	614	408	206	2·0 : 1

The figures in parentheses represent the number of cases where it was possible to confirm the address of the mother at the time of conception and early pregnancy.

It is unlikely that these urban and rural differences have resulted from chance, since the same findings are apparent in Scotland, where stillbirths are classified under the registered cause of stillbirth. The distribution of stillbirths with anencephaly as the registered cause for the years 1951–6 indicates that anencephaly is most prevalent in the lowlands around Clydeside and the Lothians (Registrar-General for Scotland Reports). Anencephaly is comparatively rare in the sparsely populated Highlands. In general, it is more common in the towns than in the rural areas, the highest incidence being in Greenock. Hence it would appear that anencephaly is related to the density of the population.

FIG. 1.—Distribution of 64 anencephalic births in Northamptonshire, 1944–57

Grouping of Births

A very definite feature of anencephaly is the way in which the births occur in groups in time and space. This was noted a hundred years ago by Del-Vesco (1859), an obstetrician in Italy, and is present in Northamptonshire to a marked degree. This grouping is illustrated in Fig. 2, from which it can be seen that, over a period of 14 years, in the village of Loddington with five births a year, the only two cases of anencephaly were born in the same year, 1950. In Cransley, with five births a year, 16 months separated the dates of the two births: in the interval a baby was born in the village with a hare-lip and palate-cleft. In Kettering 5 out of 13 anencephalics were born in one year, 1954. It is noteworthy that there were only two other anencephalics born in the county in that year. In Corby four out of eight anencephalics were born in one year, 1957. In Burton Latimer two out of three anencephalics were born in 1953. At the southern end of the industrial belt, in Higham Ferrers and Rushden, three out of five anencephalics were born in one year (1950).

The anencephalic births in Corby merit further attention. Of the four mothers who gave birth to

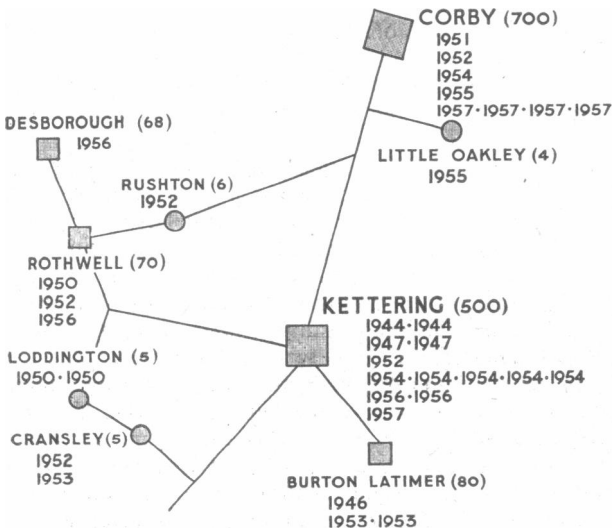

FIG. 2.—Distribution of anencephalic births in Kettering Borough and Rural District and the Urban Districts of Corby, Desborough, Rothwell, and Burton Latimer during the years 1944-57. The figures in parentheses indicate the approximate number of annual births.

anencephalics in 1957, two were living in adjacent streets during their pregnancies. Two other mothers who lived in one of these streets during pregnancy gave birth to abnormalities in 1958: in one case the baby was an anencephalic and in the other a hydrocephalic.

The dates of the births were: July 5 and October 14, 1957, and May 1 and September 14, 1958.

About a mile away two more anencephalics have been born in another street. The dates of these births were: May 29, 1955, and March 17, 1957.

It is possible that this localization of anencephalic births is due to chance, but the coincidence is so striking that it seems reasonable to accept, as a working hypothesis, the idea that they may have some common local cause.

Social Factors

Poverty is difficult to define in the Welfare State. Nevertheless, one gains the impression that anencephaly is more common among persons in the lower-income groups with large families who live in the poorer houses or areas of the town. The part of Corby referred to above, for example, contains some of the poorer dwellings; moreover, it lies in the immediate vicinity of the extensive Stewart & Lloyds steel factories. Coffey and Jessop (1957), in their inquiry in Dublin, reported an apparent association between anencephaly and unemployment and poverty. The same association with social class was noted by Edwards (1958).

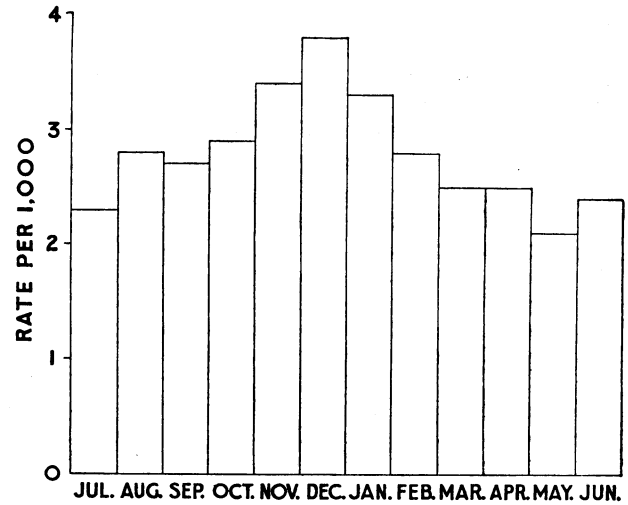

FIG. 3.—Monthly stillbirth rates attributed to anencephalus in Scotland in 1951–6.

Seasonal Incidence

The numbers of anencephalic births in Northamptonshire are insufficient to allow deductions in regard to seasonal incidence. The monthly stillbirth rates attributed to anencephalus in Scotland in 1939–46, however, were shown to exhibit a seasonal variation (McKeown and Record, 1951). The same variation is evident for the years 1951–6 (Fig. 3) (Registrar-General for Scotland, Reports for 1951–6). More cases are conceived in the summer than in the winter months.

Association of Abnormalities with Infections

From the facts presented it appears that anencephaly is associated with the density of the population and the seasons of the year and that it is more common among the lower-income groups of the population living in crowded conditions. In Northamptonshire, however, it is the grouping of anencephalic births which most attracts attention. At times anencephalic births appear to be associated with other abnormalities of the central nervous system. (Thus, for example, in the village of Bozeat, with about 17 births a year, the only congenital abnormalities recorded over a period of 14 years are one case of anencephaly and one case of spina bifida. Both were born at full term on the same day—February 23, 1947.) At other times there appears to be no association between anencephalics and other abnormalities: the anencephalics seem to form a distinct group on their own.

The environmental features which have been described could be explained if infections were commonly the cause of anencephaly and other

abnormalities. One would then expect the higher urban incidence which characterizes many infections, particularly erysipelas (Table II). One would also expect the births to be in groups: indeed, it would be strange if this were not the case, since in effect one would be noting a series of complications of an infectious process. Social factors relating to poverty and overcrowding could also be explained. At the present time, however, rubella is the only infection with which abnormalities have often been associated. Toxoplasma and syphilis are known to produce foetal abnormality, but the evidence is based mainly on individual clinical cases. An association between other maternal infections and foetal abnormalities must therefore remain largely hypothetical until more definite evidence becomes available either by retrospective or by prospective inquiry.

Retrospective Inquiry

Epidemiological

By means of retrospective inquiry Coffey and Jessop (1957) obtained evidence that mothers of anencephalics experienced more illness during the first three months of pregnancy than the mothers of controls. Retrospective inquiry from a small number of mothers of anencephalics in Northamptonshire, however, failed to reveal any history of definite febrile illness in pregnancy. The main drawback of retrospective inquiries is that reliance must be placed on the mother's memory. But despite this disadvantage epidemiological inquiry should be encouraged—especially in new towns with high birth rates—since there are occasions when abnormalities are born in a way that suggests the role of environmental factors in their aetiology.

Thus in Corby in 1957, of 850 babies born in the town, seven had a defect of the heart. Three of the seven babies were born in one street and its adjoining cul-de-sac, in which 17 babies were born in the year. A fourth baby in the street was born with hare-lip and palate-cleft. Two other babies had large naevi and another was born with bat ears. The three babies with heart defect died shortly after birth. In 1958 another baby born in this street also died from congenital heart disease (Fig. 4). In each case the heart abnormality was verified by consultant opinion or necropsy.

Congenital Disease of the Heart

Case 1.—Male. Born June 29, 1957; died August 13, 1957. Medical death certificate: cardiac failure; congenital heart disease. Post-mortem report: endocardial fibroelastosis. When the mother was three months pregnant one of her children had a feverish illness with vomiting and diarrhoea.

Case 2.—Male. Born October 3, 1957; died October 27, 1957. Consultant opinion: congenital disease of heart. When the mother was five months pregnant one of her children had chicken-pox.

Case 3.—Female. Born November 18, 1957; died March 27, 1958. Cause of death: cardiac failure; congenital heart. Seen at Great Ormond Street Hospital: opinion, tricuspid atresia. Baby appeared microcephalic. Maternal history of "three-day 'flu" in second month of pregnancy.

Case 4.—Male. Born October 6, 1958; died October 9, 1958. Post-mortem report: patent foramen ovale.

Other Abnormalities Born in the Street

Case 5.—Male. Born January 14, 1957. Naevi on cheek, leg, and finger.

Case 6.—Male. Born July 7, 1957. Bilateral bat ears.

Case 7.—Male. Born August 26, 1957. Bilateral hare-lip. (Family history of hare-lip.)

Case 8.—Female. Born December 30, 1957. Single naevus on abdomen.

This distribution of defects cannot be explained satisfactorily on the basis of chance. Yet, although a detailed inquiry was made, a history of maternal illness could be obtained in only one case (Case 3). In the course of the year some children living in the street had had chicken-pox; others had had whooping-cough. It is submitted that the most satisfactory explanation of this grouping of heart defects is on the basis of maternal infection.

Another example may be cited. In Rushden, at the southern end of the industrial belt, there were 247 live births and stillbirths in 1958. Two babies were born with congenital heart defect. In both cases the diagnosis was verified at necropsy. The two babies were born in the same street within six months of one another. Only four babies were born in this street during the year.

Serological

Another form of retrospective inquiry which may provide information is to undertake maternal serological examination after the abnormal baby has been born. In the same way that a retrospective diagnosis of enteric fever can be made on the evidence of a raised agglutinin titre, so it may be possible to obtain serological evidence which indicates previous maternal infection by one or more organisms. It is probable, however, that if infections are associated with abnormalities, the infections are common enough in the community for it to be difficult to establish a difference of statistical significance between sample and control groups. Nevertheless, an attempt seemed worth while, and with the co-operation of Professor C. P. Beattie of the toxoplasma laboratory, Sheffield, and Dr. L. Hoyle, of the Northampton Public Health Laboratory, samples of blood from mothers who had given birth to babies with abnormalities of the central nervous system were examined for antibodies to the following infections: toxoplasma, influenza A, B, and C, Q-fever, psittacosis, adenovirus, mumps, lymphocytic choriomeningitis. As control for each case a mother was selected of

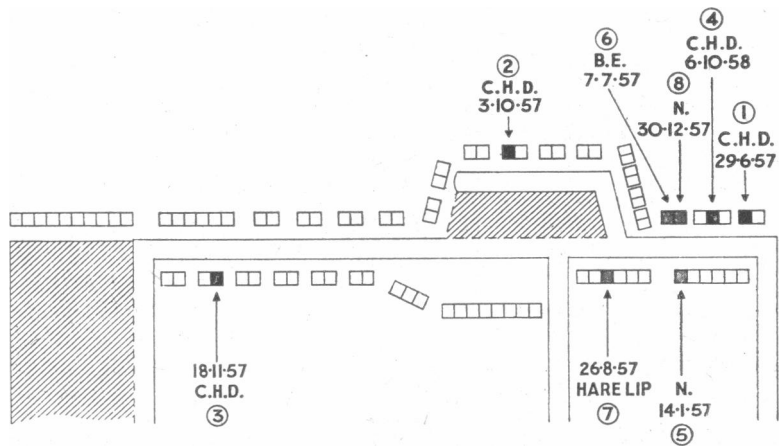

FIG. 4.—Births of abnormalities in a street in Corby New Town.

approximately the same age and multiparity and living within a distance of five miles. Similar investigations for poliomyelitis and the Coxsackie group of infections would appear justifiable in the future, but the scope of the present inquiry was limited on account of the work involved and had to be discontinued for practical reasons before any definite conclusions could be reached.

Prospective Inquiry: Asian Influenza in Pregnancy

The advantages of prospective inquiry in attempts to associate cause and event are obvious. McDonald (1958), by this means, showed that congenital abnormalities could be associated with, among other things, a higher incidence of febrile respiratory infections in pregnancy. Coffey (1958), in a preliminary report on a prospective study of 600 mothers who said they had had influenza, found that the incidence of malformed babies born to them was 3.8% as compared with 1.7% in a control group. Among 88 women who had been ill in the first trimester the incidence of congenital abnormalities was 9%. In a similar study of about 200 mothers whose diagnosis of influenza had been confirmed by a general practitioner, Doll (1958) found the incidence of congenital abnormalities to be 3%.

In Northamptonshire a small prospective inquiry was undertaken to ascertain the effects of Asian influenza in pregnancy on foetal development. Dr. C. M. Smith, the County Medical Officer, sent out a questionary to all midwives practising in the county asking them to notify details in regard to all expectant mothers under their care who suffered from Asian influenza. In response to this inquiry, notifications were received during the ensuing months of 43 expectant mothers who had fallen ill with Asian influenza. The details provided in respect of each case showed that 38 of the 43 mothers had suffered an illness severe enough to compel them to go to bed; in one case the patient could not go to bed as all the other members of the family were also affected. The length of stay in bed varied from half a day to three weeks; the average duration was five days in bed. Of the 43 patients, 33 called in their doctor. In 26 of the cases other members of the family were also affected with the same form of illness. In all but three cases the patient made a satisfactory recovery.

The illness itself as described by the midwives consisted of headache, fever, pain in the limbs, "typical influenza," and depression. No attempt was made to identify the organism responsible for the illness, and it may well be argued that there is no scientific evidence that these were cases of Asian or any other form of influenza. This reservation is accepted. It is, however, true to say that the mothers suffered from a febrile illness with symptoms and signs similar to influenza during the time when the Asian influenza reached epidemic proportions in the county.

After the notifications of the midwives had been received they were filed, and when then the baby was born some months later the details on the midwives' antenatal records and on the health visitors' birth inquiry cards were checked to ascertain whether any abnormality was present. Where an abnormality was recorded, information regarding the nature of the abnormality was obtained from the records of the medical practitioner, the medical death certificate, or the hospital records. In this way medical confirmation of each abnormality was obtained. Two cases of abortion were taken from the midwives' records.

For the purpose of controls for this series of cases the midwives were asked to send in their records for all other expectant mothers under their care who were pregnant during the period September 1 to December 31, 1957, when Asian influenza was prevalent in the county. A total of 1,040 controls were obtained in this way. In 62 cases only the midwives' antenatal records were available, but in the remainder the details of the births were analysed both from the midwives' records and from the health visitors' birth inquiry cards in the same way as in the sample group. A summary of the results in the two groups is shown in Table III. Although the figures in the sample group are probably too small to allow valid deductions to be drawn from them, it will be seen that the incidence of congenital abnormalities and abortions is higher among the sample than among the control group.

TABLE III.—*Asian Influenza in Pregnancy. Incidence of Congenital Abnormalities, Abortions, Stillbirths, and Infant Deaths as Obtained from a Prospective Inquiry in a Group of Mothers who Suffered "Asian influenza" in Pregnancy, as Compared with a Control Group*

	Sample Group	Control Group
1. Total ..	43	1,040
2. Abnormalities	3 (1 congenital heart disease. 1 spina bifida and hydrocephalus. 1 hydrocephalus)	14 (1 anencephaly. 1 hydrocephaly. 1 hydrocephaly and spina bifida. 7 congenital heart disease. 1 hare-lip/cleft-palate. 2 mongols. 1 congenital hip) In addition six minor defects were noted: 3 pyloric stenosis, 3 defects of feet
3. Abortions ..	2	10 (One occurred in a twin pregnancy)
4. Stillbirths ..	—	20 (Two occurred in twin pregnancies and one in a triplet pregnancy)
5. Infant deaths	1	8

Of 12 mothers who had Asian influenza in the first trimester, one gave birth to a baby with hydrocephalus; a second aborted at the fourth month of pregnancy; a third aborted at the sixth month of pregnancy. Of the 18 mothers who had Asian influenza in the second trimester, one gave birth to a baby with congenital heart disease. A second baby died three days after birth from bronchopneumonia. The clinical condition of this baby as described by the practitioner suggests that the cause of death may have been associated with neonatal cold injury. Of the 13 mothers who had Asian influenza in the third trimester, one gave birth to a baby with spina bifida and hydrocephalus.

Discussion

From the information presented it seems reasonable to suggest that there may be an association between Asian influenza in pregnancy and congenital abnormality. As with rubella, the risk of foetal damage appears to be greater when the illness has occurred in the early months of pregnancy, although Doll (1958) did not find this to be the case in his inquiry.

This evidence can be considered in relation to other facts which are available. Firstly, the prospective survey by McDonald (1958) showed there was an

association between congenital abnormalities and febrile illness in pregnancy, while the retrospective survey by Coffey and Jessop (1957) indicated that mothers of anencephalics experienced more illness in the first three months of pregnancy than the mothers of controls. Secondly, Lundström (1952), in his inquiry, showed that there was an increased incidence of abnormal foetuses born to mothers who had come in contact with rubella, even though they themselves had previously had rubella and gave no history of illness in pregnancy. Hence the immunity which is sufficient to protect the mother from overt illness is not necessarily sufficient to protect the foetus from attack. Thirdly, the epidemiological evidence in Northamptonshire strongly suggests that there is a much greater association between maternal infection and congenital abnormalities than is at present accepted.

Attention has already been drawn to the fact that approximately two-thirds of mongol births in Northamptonshire occur in groups (Pleydell, 1957). This distinctive grouping holds good for other abnormalities also: congenital disease of the heart, urogenital abnormalities, and orthopaedic abnormalities not infrequently occur in a manner strongly suggestive of an infectious process. Epidemiological studies of births of abnormalities—particularly in new towns with high birth rates—can produce circumstantial evidence of the causal role of infections where clinical inquiry fails to elicit a history of illness or contact with illness.

The outstanding feature of Asian influenza was the lack of native resistance to the infection. The illness sustained was generally sufficient to send the affected mothers to bed for several days. It is unlikely that this illness would have been overlocked had a retrospective inquiry been made. In fact, in cases where retrospective inquiries were made the mothers were quite definite in the information they gave, and it was generally possible to confirm the history from the general practitioner. It appears, therefore, that if the characteristic grouping of congenital abnormalities described in this paper is associated with maternal infections, such infections must be less severe to the adult than Asian influenza. The fact that we have not as yet identified them is more a reflection on our present state of ignorance than an indication that they do not exist.

The association between maternal infection in pregnancy and foetal abnormality is of the greatest importance when considering the possibility of prevention. At present public health measures can be taken to prevent an expectant mother from coming into contact with rubella; mothers who have been exposed to rubella can be protected by passive immunization with gamma-globulin. Toxoplasma is sensitive to sulphonamides. If it is confirmed that influenza in pregnancy is associated with congenital abnormality, protection may be possible by active immunization. Perhaps in the future the protection of the individual against infection will start before or soon after conception rather than shortly after birth.

In the existing scheme of antenatal care more and more attention is devoted to the expectant mother as the pregnancy advances. Little attention is paid to the early weeks of pregnancy—which are more critical for the foetus—since the mother often does not attend for examination until the second trimester. It is evident, however, that if preventive measures are to be effective there must be supervision of the early stages of pregnancy. The *British Medical Journal* (1958) advised parents who had had an anencephalic child to restrict future conceptions to the winter months. The planning of pregnancies would appear to be a rational measure for parents where there is a history of abortions, stillbirths, or abnormalities.

The evidence presented in this report draws attention to the need for further epidemiological inquiry into the cause of abnormalities. It could well be argued that it would be profitable to introduce notification and supervision in respect of the conditions which we do not understand, in place of the mild infections with which we are familiar. The recommendation in the *Lancet* (1947) that infections in pregnancy should be notifiable is as valid now as it was when it was made. Equally great is the need to maintain registers of congenital abnormalities so that accurate records can be kept in different areas throughout the country. It would appear that these administrative steps are essential if concerted measures are to be undertaken with the object of learning more about the association between prenatal infections and congenital abnormalities.

Summary

An epidemiological study in Northamptonshire provides evidence that anencephalic births are related to the density of the population. The incidence of anencephaly in urban districts is double the incidence in rural districts; the incidence in the industrial belt is three times the incidence in the rest of the county.

A definite feature of anencephalic births is that they occur in groups in time and space.

It is suggested that the association between anencephaly and social class, season of the year, density of population, and the grouping of births is best explained on the basis of an infectious causation.

A description is given of a group of births of different congenital abnormalities in one street in Corby New Town.

The results of a small prospective inquiry in Northamptonshire suggest that there may be an association between Asian influenza in pregnancy and congenital abnormalities.

Stress is laid on the importance of further epidemiological inquiries in regard to congenital abnormalities; attention is drawn to the possibility of prevention of those cases associated with infections.

I thank Dr. C. M. Smith, County Medical Officer of Health, Northamptonshire, for his advice and encouragement in undertaking this survey; Dr. McKinlay, from the Department of Health for Scotland, for providing me with statistics of the incidence of anencephaly in Scotland; and the consultant paediatricians and obstetricians who let me see their records. I am indebted to the doctors who provided me with information in many cases; to the health visitors and district-nurse midwives for their conscientious inquiries on my behalf; and to the staff of the health department and the hospitals for the help they gave me.

REFERENCES

Brit. med. J., 1958, **1**, 695.
Coffey, V. P (1958). *Brit. med. J.*, **2**, 910.
—— and Jessop, W. J. E. (1957). *Brit. J. prev. soc. Med.*, **11**, 174.
Del-Vesco, P. (1859). *Gazz. med. ital. prov. venete, Padova*, **2**, 149. Cited by J. W. Ballantyne, *Antenatal Pathology and Hygiene: The Embryo*, p. 336. Green, Edinburgh, 1904.
Doll, R. (1958). *Brit. med. J.*, **2**, 910.
Edwards, J. H. (1958). *Brit. J. prev. soc. Med.*, **12**, 115.
General Register Office (1954). Census 1951. England and Wales: County Report, Northamptonshire. H.M.S.O., London.

Lancet, 1947, **1**, 639.
Lundström, R. (1952). *Acta paediat. (Stockh.)*, **41**, 591.
McDonald, A. D. (1958). *New Engl. J. Med.*, **258**, 767.
McKeown, T., and Record, R. G. (1951). *Lancet*, **1**, 192.
Penrose, L. S. (1955). Malformations detectable at birth and their relation to fresh mutation (unpublished memorandum).
Pleydell, M. J. (1957). *Lancet*, **1**, 1314.
Registrar-General for Scotland, Reports for 1951–6.

PREVENTION OF STAPHYLOCOCCAL SEPSIS IN A MATERNITY HOSPITAL BY MEANS OF HEXACHLOROPHANE

BY

K. SIMPSON, M.D., M.R.C.P.
Senior Paediatric Registrar

ROSEMARY C. TOZER, B.Sc.
Bacteriologist

AND

W. A. GILLESPIE, M.A., M.D., F.R.C.P.I., D.P.H.
Clinical Pathologist

United Bristol Hospitals

In a previous paper (Gillespie *et al.*, 1958) we showed that infants who became heavily colonized by *Staphylococcus aureus* within a day or two of birth subsequently developed septic lesions of the skin more often than other infants. This tendency was particularly pronounced with staphylococci of phage patterns 52A/79 and 80, which were the most virulent strains prevalent in the hospital. The application to the umbilical area of a dusting powder containing hexachlorophane greatly reduced the staphylococcal colonization of the umbilicus and groin, and reduced the colonization of the perineum and nose to a smaller extent.

We report here some further results obtained in the same investigation. The clinical and bacteriological effects of applying hexachlorophane powder from earlier in life and to a wider area of skin were studied. Changes in nursery routine which reduced the contacts between infants and nurses were investigated.

The basic nursery techniques were described in our previous paper. Some changes then introduced were continued: namely, the disinfection of blankets and garments; the use of hexachlorophane soap for hand-washing; and the sealing, with "octaflex," of umbilical-cord stumps, which were then left uncovered. Chlorhexidine ("hibitane") hand-cream was withdrawn, however, so as to simplify the present trial.

Effect of Hexachlorophane Powder

Fig. 1 shows the results of direct plating of swabs taken from the carrier sites of most infants admitted to nurseries 2 and 3 of the Bristol Maternity Hospital. (Swabs from infants treated with hexachlorophane were soaked before use in 1% "tween 80" broth and plated on nutrient agar similarly fortified.) Enrichment culture in salt meat broth gave slightly more positive cultures but did not affect the general patterns of the graphs. From February 26 until August 17, 1958, hexachlorophane powder ("ster-zac") was applied to the umbilicus and the front of the abdomen of every infant admitted to nursery 2, and this was repeated every time the napkin was changed, until the cord separated. From August 18, 1958, until June 15, 1959, the infants were first powdered in the labour room before they went to nursery 2, and the powder was applied repeatedly to the whole trunk, including the buttocks, perineum, axillae, and groins as well as the umbilicus, until the infants left hospital. The more liberal use of the powder did not improve the protection of the umbilicus and groin, but perineal and nasal colonization was further reduced (Fig. 1). In nursery 3, where no powder was used until February 13, 1959, the colonization of all four carrier sites continued at much higher levels than in nursery 2 (Figs. 1 and 2).

After the introduction of powdering of the umbilical area, the incidence of staphylococcal lesions of the skin fell from 19/365 (5.2%) to 7/343 (2.0%) (see Table).

Effect of Hexachlorophane Powder on the Incidence of Staphylococcal Skin Lesions

	Nursery 2			Nursery 3
	7/7/57–24/1/58	26/2/58–17/8/58	18/8/58–15/6/59	19/5/58–12/2/59
Area powdered ..	None	Umbilicus	Whole trunk	None
No. of infants ..	365	343	554	464
,, with skin sepsis	19 (5·2%)	7 (2·0%)	5 (0·9%)	34 (7·3%)

The difference was statistically significant ($\chi^2 = 5.0$; $P < 0.05$). Subsequently, with the more liberal use of the powder, the incidence of sepsis fell again, to 5/554 (0.9%). In the control nursery 3 the incidence of sepsis in a comparable period remained high, at 7.3% (see Table), and there occurred a small outbreak of pemphigus neonatorum caused by a penicillin-resistant

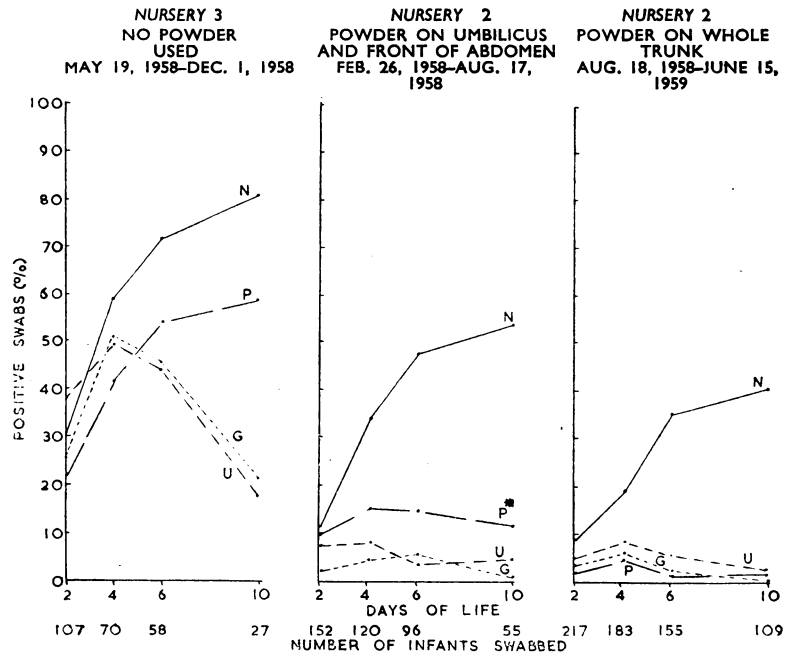

FIG. 1.—Effect of hexachlorophane powder on staphylococcal colonization of infants. N=Nose. P=Perineum. U=Umbilicus. G=Groin. *Perineal swabs were not taken before May 3. Numbers of perineal swabs on 2nd, 4th, 6th, and 10th days were 96, 75, 63, and 32 respectively.