SUBSEQUENT INFECTION OF INFANTS BORN IN A MATERNITY HOSPITAL

A TRIAL OF A STAPHYLOCOCCAL VACCINE AND TOXOID AND A STUDY OF THE RELATION BETWEEN INFECTION IN THE MATERNITY HOSPITAL AND SUBSEQUENT INFECTION

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This inquiry had three purposes. First, to discover whether certain immunization procedures carried out in the first two days of life lessened the incidence of visible septic lesions in infants in the first ten days of their lives, during their stay in the maternity hospital where they were born. Secondly, to see whether the immunization procedures affected the incidence of diagnosed infections in the babies after their discharge from the hospital up to the age of 3 months. Thirdly, to find out whether the babies who showed visible septic lesions while in hospital fared better or worse as regards infection during the first 3 months than the babies who showed no septic lesions while in hospital.

Material and Methods

The investigation was carried out with the consent of the mothers, on babies born in the Weir Maternity Hospital, Balham, London, between July 3, 1960 and September 29, 1962; only those weighing 5 lb. (2.26 kg.) at birth and appearing to be normal and healthy were included.

The Weir Hospital contains 54 beds in wards varying in size from single rooms to 12-bedded units of which there are two. For the purpose of the investigation the whole hospital was considered as one unit, reliance being placed on large numbers to iron out differences that might be attributable to having the children in different wards. The policy of rooming-in is in force at the hospital and no change was made during the period of the trial in the existing and customary arrangements employed to minimize the spread of infection. No antiseptic substances are applied to the babies' skins, and no dressing is used on the umbilical stumps.

The babies were divided into three groups. Group A consisted of those whose mothers' surnames began with the letters A-J inclusive. The names in Group B began with the letters K-Q inclusive, and in Group C with R-Z inclusive.

All three groups were given two intramuscular injections, the first as soon as possible after birth (all within 24 hours), and the second approximately 24 hours later.

The Vaccine. This was given to Group A. Each dose consisted of 0.1 ml. of a sterile suspension of killed staphylococci, there being approximately 50 million organisms in each millilitre. Half the organisms in the suspension were of Phage type 80, and half of Group 3 (Phage types 6, 7, 47, and 54). Details of the preparation of this vaccine, which was made in the Bacteriology Dept. of St. James' Hospital, Balham, London, will be supplied on request.

The Toxoid. This was given to Group B, each dose consisting of 0.1 ml. of the B.P. Staphylococcal Toxoid purchased from Burroughs Wellcome.

The Controls. Group C received 0.1 ml. sterile water in each injection, and provided the controls.

Observations were made on all the babies in the series who remained in hospital for 10 days—the normal period of stay. The midwifery staff had been asked to look for septic lesions as opportunity arose, but not to undress the babies specially for this purpose. A member of the paediatric resident staff confirmed the midwife's observation and entered the site and nature of the first lesion to be noted in a book provided for the purpose. Nil entries were made for the babies who did not show any septic lesion.

Results

The series comprised 2,782 babies, of which 1,217 were in Group A, 867 in Group B, and 698 in Group C. No ill effects attributable to the injections were noted. Table 1 gives an anatomical and numerical summary of the septic lesions recorded in each of the three groups. It will be seen that septic lesions

TABLE 1
VISIBLE SEPTIC LESIONS DURING THE FIRST TEN DAYS
OF LIFE, WHILE IN THE MATERNITY HOSPITAL

Site	Vaccine	Toxoid	Control	Total
Eye	55	49	41	145
Skin	62	39	33	134
Digits	2	3	0	5
Umbilicus	3	1	2	6
Breast	0	1	1	2
Nose	1	0	0	1
Cellulitis	0	1	0	1
Ear	0	1	0	1
Urine	0	0	1	1
Total	123	95	78	296

appeared in 123 out of 1,217 (10.1%) babies in Group A; 95 out of 867 (10%) in Group B, and 78 out of 698 (11%) in Group C. These findings show that neither the vaccine nor the toxoid was effective in reducing the incidence of visible septic lesions in the babies while they were in hospital.

The Follow-up. While they were still in hospital, the mothers of the babies in the series were given a questionnaire, were shown how to complete it, and were given a stamped addressed envelope. They were asked to answer the questions when the baby reached the age of 12 weeks and to post it to the author.

The services of the Health Visitors were kindly made available by the Medical Officer of Health for Battersea and Wandsworth, Dr J. H. Tudor Lewis. The names and addresses of mothers who had not sent in their replies at the proper time were sent to him, and he requested the Health Visitor to call and help the mother to answer and post the questionnaire. The questionnaire contained three questions relating to the period between the tenth day of discharge and reaching the age of 12 weeks. Unfortunately the

hoped-for precision of the follow-up period was blurred by the fact that a number of the replies were not received until the baby was more than 12 weeks old. This must be born in mind when considering the results.

The questions were:

1. Has your baby had any minor ailments which were cured or cured themselves without medical advice?
2. Has your baby had any illness for which your doctor was consulted? If so please ask your doctor to help you to state the diagnosis with the dates and a brief note if possible. If none please state 'None'.
3. Has your baby had any illness for which removal to hospital was necessary? If so please give any details you can and the name of the hospital to which your baby was sent. If none please state 'None'.

A total of 1,476 (53%) replies was received. Of 1,217 Group A mothers, 640 (52.5%) replied; of the original 867 Group B mothers, 485 (55.7%) replied, and of the original 698 Group C mothers, 351 (50.2%) replied. The proportion of replies from the mothers of the babies who showed a septic lesion in the maternity hospital was particularly disappointing, 106 (35.8%) replies being received from among the 296 mothers in this category. A septic lesion had been seen in hospital in 70 (12.1%) of the infants of the 577 mothers in Group A who did not reply. The corresponding figure for the 382 mothers in Group B who did not reply was 65 (17%), and for the 347 non-replying mothers in Group C the figure was 55 (15.8%). There is no means of finding out the reason for the uneven distribution of visible septic lesions among the three groups of the mothers who did not reply, so that this must remain the subject of conjecture. The low over-all reply rate is almost certainly a reflection of the instability of the population of mothers who are delivered in London. The above observations regarding the replies to the questionnaire suggest that the results of the follow-up and the conclusions drawn from them require confirmation by further and more complete studies.

Table 2 gives a numerical and approximate diagnostic summary of the babies in each group who, though they showed no visible septic lesion during the first 10 days, did develop a diagnosed infection during the follow-up period. The diagnostic summary is approximate only because of the difficulty of presenting the data in detail. Some of the babies developed more than one infection, mostly respiratory, and only a cumbersome table could give the full history of the cases. The figures in brackets indicate the number in each category who also developed a respiratory infection. Where other infections are

TABLE 2
INFECTIONS DEVELOPED DURING FOLLOW-UP PERIOD
IN BABIES WHO SHOWED NO VISIBLE SEPTIC LESION
WHILE IN HOSPITAL

Diagnosis	Vaccine	Toxoid	Control	Total
Respiratory	142	99	80	321
Eye	52 [10]	22 [10]	24 [5]	98
Skin	17 [3]	18 [3]	12 [2]	47
Digits	5 [5]	3 [2]	3	11
Breast	4	0	0	4
Umbilicus	1 [1]	1	0	2
Ear	2	1	0	3
Glands lymph	1	0	0	1
Enteritis	1	2	1	4
Whooping cough	2	0	0	2
Measles	3	0	0	3
Rubella	4	1	1	6
Chicken-pox	0	2	0	2
Meningitis	1	0	0	1
Total	235	149	121	505

Figures in brackets indicate the number who also had a respiratory infection.

TABLE 3

INFECTIONS DEVELOPED DURING FOLLOW-UP PERIOD
IN BABIES WHO SHOWED VISIBLE SEPTIC LESIONS
IN HOSPITAL

Diagnosis	Vaccine	Toxoid	Control	Total
Respiratory ..	9	11	4	24
Eye ..	9 [1]	2 [1]	3 [1]	14
Skin ..	6	3	0	9
Digits ..	0	2	1	3
Breast ..	0	0	1	1
Gland/lymph ..	1	0	0	1
Enteritis ..	1	0	0	1
Chicken-pox ..	1	0	0	1
Total ..	27	18	9	54

Figures in brackets indicate the number who also had a respiratory infection.

TABLE 4

NUMBERS OF BABIES SHOWING VISIBLE SEPTIC
LESIONS IN HOSPITAL AND WHO DID NOT DEVELOP A
DIAGNOSED INFECTION DURING THE
FOLLOW-UP PERIOD

Vaccine	Toxoid	Control	Total
26	12	14	52

TABLE 5

NUMBERS OF BABIES SHOWING NO VISIBLE SEPTIC
LESIONS IN HOSPITAL AND NOT DEVELOPING
DIAGNOSED INFECTION DURING FOLLOW-UP

Vaccine	Toxoid	Control	Total
352	306	207	865

concerned the case has been counted under the heading which, from the reply, seemed to the author to be the most significant (e.g. a baby who had a septic spot and a whitlow would be listed under 'whitlow' and not under 'skin'). This nosological classification must therefore be taken only as a rough indication of the picture, but as no baby has been entered more than once the grand totals are valid for statistical purposes. It will be noted that this Table

TABLE 7

NUMBERS OF BABIES DYING DURING FOLLOW-UP
WHOSE DEATHS WERE PRESUMED TO HAVE BEEN
CAUSED BY INFECTION. CASES CLASSIFIED ACCORDING
TO WHETHER OR NOT THEY HAD SHOWN SEPTIC
LESIONS WHILE IN MATERNITY HOSPITAL

Diagnosis	Vaccine		Toxoid		Control	
	No Sepsis	Sepsis	No Sepsis	Sepsis	No Sepsis	Sepsis
Meningitis	1	0	0	0	0	0
Pneumonia	4	0	0	0	1	0
Total ..	5	0	0	0	1	0

includes babies with diseases such as the infectious fevers, which one would assume to be of virus origin; moreover many of the respiratory infections might well have been of virus origin. It should also be noted that the severity of the incident is not taken into account. These points will be dealt with in the discussion.

Table 3 gives a numerical and diagnostic summary of the babies in each group who had shown a visible septic lesion while in hospital, and who also developed a diagnosed infection during the follow-up period.

Table 4 gives the number of babies in each group who had shown a visible septic lesion while in hospital, but had developed no diagnosed infection during the follow-up period.

Table 5 gives the number of babies in each group who had shown no visible septic lesion while in the hospital and who developed no diagnosed infection during the follow-up period.

From Tables 2 and 5 it is calculated that of 351 babies in the control group, 130 (37%) developed a subsequent infection. Of a total of 640 babies who received the vaccine, 262 (40.9%) developed a subsequent infection ($p = 0.3$). From these Tables it can also be calculated that, of 485 babies who received the toxoid, 167 (34.4%) developed a subsequent infection ($p = 0.5$).

From this it can be concluded that neither the

TABLE 6

INFECTIONS DEVELOPED DURING FOLLOW-UP, WHICH WERE NOT FATAL BUT WERE
SEVERE ENOUGH FOR ADMISSION INTO HOSPITAL, CLASSIFIED ACCORDING
TO WHETHER OR NOT THE BABIES HAD SHOWN SEPTIC LESIONS IN MATERNITY HOSPITAL

Diagnosis	Vaccine		Toxoid		Control		Totals
	No Sepsis	Sepsis	No Sepsis	Sepsis	No Sepsis	Sepsis	
Bronchitis ..	2	0	2	1	2	0	7
Bronchitis and otitis ..	1	0	0	0	0	0	1
Tracheo-bronchitis ..	1	0	0	0	0	0	1
Pneumonia ..	0	0	1	0	0	0	1
Gastro-enteritis ..	2	1	1	0	0	0	4
Breast abscess ..	1	0	0	0	0	0	1
Abscess of neck ..	1	0	0	0	0	0	1
Infected scalp ..	0	0	1	0	0	0	1
Whitlow ..	0	0	0	1	0	0	1
Total ..	8	1	5	2	2	0	18

vaccine nor the toxoid, in the doses and timing used here, were effective in reducing the incidence of subsequent infection during the follow-up period.

Prevention of Severe Subsequent Infection. The true purpose of an immunization programme such as this is to prevent the occurrence of infections severe enough to be regarded as serious. A crude but easily applied definition of severity was chosen for the purpose of this investigation. Infections were classed as severe if they either necessitated the admission of the baby to hospital, or if they brought about the baby's death.

Table 6 gives a diagnostic summary of the babies in each group who developed severe subsequent infections. It also indicates whether or not the case had shown any visible septic lesion while in the Maternity Hospital. Table 7 gives the same information about the babies who died from diseases which must be presumed to be the result of infection.

From Tables 6 and 7 it is seen that of 351 babies in the control group, 3 (0.8%) developed severe subsequent infection; of 640 babies who had received the vaccine, 14 (2.1%) developed severe subsequent infection ($p = 0.2$). Of 485 babies who had received the toxoid, 7 (1.4%) developed severe subsequent infection ($p = 0.5$). From this it can be concluded that neither the vaccine nor the toxoid had a significant effect on the incidence of severe subsequent infection.

Of 351 babies in the control group, one (0.2%) died; 5 vaccine babies died (0.7%) ($p = 0.5$); and none of the toxoid babies died ($p = 0.5$). It is thus clear that neither the vaccine nor the toxoid had a significant effect on the death rate of the babies.

Prognosis for Babies Showing Septic Lesions While in the Maternity Hospital. Having demonstrated the inefficacy of the vaccine and the toxoid it is now possible to assess the influence of hospital sepsis on the subsequent fate of the babies, and to find out whether the development of a septic lesion in the Maternity Hospital carries an increased risk of infection of any kind, of severe subsequent infection, or of death from infection.

From Tables 3 and 4 it will be seen that of 106 babies who showed a septic lesion while in hospital, 54 (50.9%) developed a subsequent infection, whereas of 1,370 babies who did not show any septic lesion in the hospital, 505 (36.1%) developed subsequent infection ($p = 0.05$). From this it can be concluded that sepsis in the Maternity Hospital does carry an increased risk of subsequent infection.

From Tables 6 and 7 it will be seen that of 106 babies showing sepsis in hospital, 3 (2.8%) developed

severe subsequent infection, compared with 21 (1.5%) out of 1,370 babies who did not show any hospital sepsis ($p = 0.5$).

Sepsis in Maternity Hospital and Subsequent Death from Infection. From Table 7 it is seen that none of the babies who died from infection had shown a septic lesion while in the Maternity Hospital, and that the 6 deaths from this cause came from among the babies who had not shown any septic lesion while in the hospital. This number of deaths is too small for any firm conclusion to be drawn, but it is nevertheless interesting to note that all of the deaths did fall into the 'no sepsis' group.

Case Histories

The following are case histories of those babies who died.

Case 1. A male baby given vaccine (born August 9, 1960) had been taken to the doctor on four occasions (no dates given) for 'crying in the night'. No cause had been found. He had appeared quite well until found dead in the early hours of November 25, 1960. Necropsy showed acute meningitis (no bacteriology available). Age at death 108 days.

Case 2. A female control baby, born May 29, 1961. No complaints of any kind. She was found dead in the early hours of June 15, 1961. Necropsy showed bronchopneumonia. Age at death was 17 days.

Case 3. A male baby given vaccine (born October 10, 1961) had two septic fingers during the first week after leaving hospital: both cleared completely. He had seemed very well until the day of death when he was found blue and hardly breathing. When taken to hospital his temperature was found to be 87° F. (30.6° C.). Widespread bruises and multiple paronychia. He died on November 9, 1961 shortly after admission. Clinical diagnosis was septicaemia. Necropsy showed pneumonia. Blood taken from the heart after death grew *Staph. pyogenes*. Age at death was 30 days.

Case 4. A male baby given vaccine (born on November 8, 1961), on December 30 had cough and cold, and the doctor diagnosed inflamed throat. He made an apparently complete recovery on medicine. On January 20, 1962 the baby was found dead in his cot having appeared to be perfectly well when last put down. Necropsy showed acute pneumonia. Age at death was 42 days.

Case 5. A male baby, given vaccine (born December 25, 1961) had a cold on February 11, 1962. A murmur had been heard in the heart and the baby was awaiting a hospital appointment for this. On March 20, coryza; feeding well no signs in chest. Following day refused some feeds but did not look ill; afebrile. On evening before admission to hospital he was noticed to be cold

and quiet: heart was beating slowly with poor breathing. On March 24, 1962 he was admitted to hospital. Temperature was 82·6° F. (28·1° C.). Crepitations in right lung; no murmur. Blood sugar 10 mg./100 ml. Blood culture *Strep. pneumoniae*. Nose and throat cultures *Staph. pyogenes*. A few hours after admission he regurgitated and collapsed. Clinical diagnosis was hypothermia, congenital heart disease, and ? pneumonia. Necropsy revealed tricuspid stenosis and patchy congestion of lungs. Age at death was 89 days.

Case 6. A baby girl given vaccine (born January 15, 1962) had no complaints until morning of death when she was found limp and cold, and died on the way to hospital. Necropsy revealed bronchopneumonia. Lung culture grew *Staph. pyogenes*. Age at death was 101 days.

Discussion

'A germ free world is an ecological absurdity, just as a perpetual motion machine is a mechanical absurdity.' Sir Julian Huxley (1963).

'If I had my way I would implant man with a known concoction of living infective agents under controlled conditions rather than let him go germ free into a world, which I cannot conceive will ever become germ free.' H. Koprowski (1963).

Infection of newborn babies in maternity hospitals would not receive the attention it does were it not for the fact that from time to time the lesion shown by a baby or group of babies, instead of being trivial and self limiting, such as a small pimple or 'sticky eye', proves to be severe or even fatal, such as septicaemia, osteomyelitis, or pneumonia. Such occurrences are not common. Forfar, Balf, Elias-Jones, and Edmunds (1953) described 6 (0·2%) very severe cases occurring in babies shortly after birth in a total of 2,389 babies born in two maternity units. Sometimes outbreaks occur, and these are usually associated with what are regarded as particularly virulent organisms like the Type 80 staphylococcus.

Bacteriological forecasting involving regular routine swabbing of staff and patients is not generally regarded as a practicable or effective means of forestalling such outbreaks, and those who have to advise on the care of babies in maternity units rely on two other approaches to the problem of preventing severe infection in the babies. On the one hand overt infections, however trivial they may appear, are all regarded as potentially lethal, prompt bacteriological investigation is carried out, and the case is watched carefully in isolation until it is cured, usually without, but sometimes with, antibiotics. Meanwhile an attempt is made, by the use of classical aseptic techniques, and sometimes also by applying antiseptics to their skins, to prevent germs from gaining access to the bodies of the babies.

The success of the aseptic measures can be judged

from the published figures. Those showing the rate of colonization of newborns with staphylococci vary from 65% (Williams, 1961) to 100% (Cunliffe, 1949) by the end of the first ten days of life. Sepsis rates reported from units of differing magnitude vary from 4% to 29%, most of the figures ranging between 10% and 20% (Williams, Blowers, Garrod, and Shooter, 1960), and it is within the experience of many that an outbreak of sepsis has forced the closure of a reputable unit.

The antiseptic approach has shown some success. Corner, Crowther, and Eades (1960) reported a skin sepsis rate of 1·5% in a maternity unit after introducing a hexachlorophene skin routine. Before its use the rate for 'skin sepsis and abscess' was 7·4%. The corresponding rates for premature babies were 2·6% and 15%.

Gluck and Wood (1961) reported a nasal colonization rate of 30% and an umbilical colonization rate of 42% before the introduction of a hexachlorophene washing routine. The rates after its introduction were 2% and 1% respectively. They do not, however, report the incidence of visible sepsis, and one has to infer a corresponding reduction in this. Neither of these workers had followed up the babies.

We must ask ourselves what it is we are trying to achieve. If the object is to prevent germs from gaining access to newborn babies while they are still in hospital, it appears that the antiseptic approach, though not perfect, is more promising than the aseptic one. But if we are trying to prevent babies from being made seriously ill or dying from infection, are we justified in assuming that preventing germs from gaining access to them while in hospital, will achieve this objective? Is it correct to assume that a low colonization or visible sepsis rate in hospital will lessen the incidence of serious or fatal subsequent infection?

It was with these thoughts in mind that the present investigation was undertaken. A previous study in the Weir Maternity Hospital of 1,830 newborn babies showed a sepsis rate of 10% (Burkinshaw and Kippax, 1958, unpublished). Coagulase-positive staphylococci were grown from 118 out of a total of 152 babies who developed skin lesions, from 93 out of 137 who developed conjunctivitis, and from 16 out of a total of 20 lesions at other sites. No bacteriological findings are recorded for the present investigation, but there is no reason to suppose that the findings would differ substantially from those of the previous study.

The two injections given in the present investigation were given within the first 3 days, not because this timing had much to recommend it at the time when this study was being planned, but because it

seemed to be a timing that might conceivably help the newborn baby in his presumed early encounter with the staphylococcus. The results show beyond doubt that neither the vaccine nor the toxoid had any effect, beneficial or otherwise in the neonatal or follow-up periods. It is nevertheless encouraging, since this study was completed, to receive some laboratory support for our empirical approach from the work of Smith, Eitzman, Catlin, Wirtz, and Miller (1964). These workers, using a salmonella antigen, report the appearance in newborn babies of one kind of flagellar antibody, in some infants by the seventh day, and in 80% by the fourteenth day. A second and different antibody was found in the infants between the 30th and 40th days.

Having disposed of the vaccine and the toxoid, we may consider the relation between a septic lesion in the maternity hospital and subsequent infection. Three possibilities come to mind. On the one hand a septic lesion acquired in the hospital might stimulate the immune responses of the baby and so lessen the chances of its developing signs or symptoms of infection during the follow-up period. Or, the appearance of a septic lesion in the neonatal period might serve as a warning of serious trouble to come. The third possibility is that the appearance of a septic lesion in a newborn might serve to distinguish a certain type of baby who, though showing a proneness to minor infections, does not necessarily have an increased susceptibility to severe subsequent infection.

The present findings show that the presence of a septic lesion in the hospital carries a significantly higher risk of subsequent infection. The figures for morbidity from subsequent infection, though high, do not reflect the severity of the illnesses which it caused. Most of the cases listed under the heading *respiratory infection* were described in words like 'just a cold' or 'slight catarrh', and in many cases the parent had not even consulted the doctor. Though tempting to subdivide the cases according to severity, it was impossible to find a reliable criterion. Most of the subsequent skin and eye infections were also of a slight and self-limiting type. Virus infections were inevitably included, partly because of lack of any means of knowing for certain the nature of the infecting organism, and partly because the purpose of the investigation was to try to assess the reactions of the babies to whatever infections they encountered—both bacterial and viral—rather than the response to any particular organism.

When the relation between hospital sepsis and severe subsequent infection is examined, it seems that the risk to the babies who showed septic lesions in hospital was not significantly greater than to those

who did not. In this connexion it is interesting to note that in only 2 out of the 6 severe cases reported by Forfar *et al.* had there been a septic lesion in the maternity unit. The figures in the present series relating to death in the follow-up period are statistically not entirely satisfactory owing to the small numbers, but at least they are reassuring in a negative way. With this reservation, the evidence here presented suggests that sepsis in hospital, though it does carry an increased probability of subsequent infection, does not indicate an increased likelihood of severe or fatal subsequent infection.

The Problem of Virulence and Susceptibility.

Experimental work in man with the staphylococcus shows how hard it is to arrive at any absolute standard of virulence. In a classical experiment Garre (1885, quoted by Elek, 1959) failed to produce any effect when he inoculated the scarified bed of his finger-nail with organisms from a colony isolated from a fatal case of osteomyelitis; and in order to produce a carbuncle had to rub into the skin an entire slope culture of the same organism. Elek and Conen (1957) found that it took from one to five million staphylococci, grown from pyogenic lesions, to produce pus formation at the site of intradermal injection in healthy adult volunteers, and that less than one million organisms produced transient reddening and swelling only. The minimum pus-forming dose is very much larger than that which would be present in any naturally occurring droplet or dust-borne infection. Three strains of staphylococcus from lesions and 9 strains from nasal carriers were tested with paired volunteers and no differences in virulence, as judged in this way, could be detected. They did, however, show that the minimum pus-forming dose was greatly reduced by the foreign body reaction provoked by skin sutures.

During outbreaks of infection in hospitals by reputedly virulent organisms, only some of the babies fare badly; most of them fail to develop any disease. This observation and the work quoted above bring us back to the question of susceptibility. Can we pick out in advance those babies who are likely to be made dangerously or fatally ill by infection? Do such babies differ from others in any measurable respect?

When compared with the volume and nicety of existing knowledge of the mechanisms of immunity and of the sources and modes of spread of infection, our knowledge of the facts concerning increased susceptibility is fragmentary. We believe that such factors as senility and prematurity, blood dyscrasias, starvation, tissue damage, diabetes, uraemia, agammaglobulinaemia, and possibly emotional factors increase susceptibility to bacterial infection,

and that babies with infantile eczema may fare badly when they encounter the virus of vaccinia and herpes simplex. We also know something about the passage of antibodies across the placenta. But we have no way of picking out the newborn with increased susceptibility to infection. In this context the comment of Smith *et al.* (1964) on their results with salmonella antibodies is interesting. They suggest that, 'genetic and developmental alterations in the sequences of antibody production could be implicated in as yet unexplained allergic disorders of infancy and early childhood'.

The Deaths. The staphylococcus was certainly responsible for two of the deaths. It was cultured from the nose and throat of Case 5, but a different organism was recovered from the blood. The important feature which 5 of the 6 cases have in common is the suddenness and unpredictability of their terminal illness (cot deaths). Two of these babies had successfully overcome a skin infection earlier in their lives, and yet were overwhelmed suddenly. If the cause of their death was a virulent organism acquired in the maternity hospital, why did they not die sooner, and why did not more babies become seriously ill?

While persevering with accepted methods in our attempts to minimize and prevent serious illness or death from infection, the emphasis in research should now shift from devising means of preventing germs from reaching the babies to investigating the mechanism of increased susceptibility.

Summary

A series of 2,782 newborn babies born in the Weir Maternity Hospital has been studied from the point of view of infection during the first ten days of life. 1,476 of them have been followed by means of a questionnaire, up to about the age of 3 months.

It is shown that babies who develop a septic lesion while in hospital have a significantly greater incidence of subsequent infection, but that there is no such correlation in respect of severe subsequent infection, or of death from infection during the follow-up period.

It is shown that a staphylococcal vaccine and a staphylococcal toxoid in the dose and timing employed failed to diminish the incidence of septic lesions in the first 10 days while in hospital, or of subsequent infection, severe subsequent infection, or of death from infection during the follow-up period.

Of the 6 babies who died from presumed infection, 5 had been thought to be in good health up to the time when they were found dead or dying in their cots. None of the babies who died had shown a septic lesion while in hospital.

The problem of increased susceptibility to infection is discussed; the practical value of attempts to prevent bacteria from gaining access to newborn babies is doubted; and a plea is made for research into the mechanism of increased susceptibility.

It is a pleasure to acknowledge the help received from the midwives of the Weir Hospital, whose cheerful co-operation and acceptance of much extra work were a *sine qua non* for this investigation; from successive members of the paediatric resident staff who gave the injections and collected the data on the newborn babies from the members of the bacteriological staff of St. James' Hospital, Balham, headed by Dr. P. W. Kippax, who prepared the vaccine; from the Health Visitors of the Boroughs of Wandsworth and Battersea, who visited many of the mothers in their homes; from the many general practitioners who helped the mothers to complete the questionnaires; from Dr. J. Luder, Dr. F. Nash, and Dr. O. Fisher for supplying details about Cases 3, 5, and 6, and from the parents for providing the babies, allowing us to inject them, and for taking the trouble to complete and return the questionnaires.

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