

THE SOURCE OF INFECTION IN PEMPHIGUS NEONATORUM

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(With 2 Figures in the Text)

In 1946 several cases of pemphigus neonatorum due to *Staphylococcus aureus* occurred in a maternity unit. The Public Health Laboratory, Carmarthen, was asked to investigate the outbreak, and this provided an opportunity to use the method of bacteriophage typing in an attempt to trace the source of infection. Dr V. D. Allison, of the Central Public Health Laboratory, Colindale, kindly provided us with a series of bacteriophage filtrates prepared according to the method of Wilson & Atkinson (1945). A large number of strains of *Staph. aureus* had been collected during a period of intensive investigation and 210 of these were tested against the phage filtrates.

DESCRIPTION OF THE OUTBREAK

The maternity unit in which the outbreak occurred had a normal capacity of twenty-five beds. Owing to lack of space there was a good deal of unavoidable overcrowding, especially in the nursery. The babies were mainly accommodated in one room measuring 14 ft. by 24 ft., which was so badly designed that only about one-half of the floor space could be used for the cots. In addition, there was another small room with two cots for premature infants. The numbers in the nursery fluctuated between fifteen and twenty-five during the period of this investigation. About one in three of the mothers and their babies were transferred to a separate Maternity Annexe on the 2nd or 3rd day of the puerperium, and most of the remainder were discharged to their homes on the 9th or 10th day. Thus, the nursery population had a low average age and a greater rate of turnover than is usual.

The first case of pemphigus for many months occurred in the middle of March 1946, and there were eighteen in all before the outbreak ceased in the first week of August. After this there were no more cases during the rest of the year. Other septic lesions due to *Staph. aureus* were not prevalent, as only one case of external otitis was seen among the infants during the year. No breast abscesses or other septic lesions occurred among the mothers in hospital, and no whitlows or skin infections were reported from the staff.

Clinically, the cases of pemphigus were mild. Most were detected at the stage when only one bullous lesion was present, and prompt local treatment with penicillin resulted in the rapid recovery of all cases. Thus, within the nursery the disease was little more than a mild nuisance. However, a number of further cases developed among babies who had recently been discharged from hospital. The treatment of these was often considerably delayed, and generalized pemphigus occurred. It was thus considered important to control the outbreak.

Cases of conjunctivitis ('sticky eye') occurred throughout the year, but were not unduly prevalent during the outbreak of pemphigus. *Staph. aureus* was isolated from nineteen of the thirty-six cases. All were mild, and the staphylococcal cases were not clinically distinctive.

Mild diarrhoea was prevalent in the nursery during the summer and autumn. This began at about the same time as the pemphigus but continued for some time after its subsidence. It was found that *Staph. aureus* could be isolated as frequently from the faeces of healthy contact infants as from the cases of diarrhoea and pemphigus. *Staph. aureus* was grown from approximately half of all the specimens of faeces by the use of 7% salt mannite agar plates (Chapman, 1945).

The weekly occurrence of cases of pemphigus neonatorum and of 'sticky eye' is shown in Fig. 1.

BACTERIOLOGICAL INVESTIGATIONS

Material from all cases of pemphigus and of 'sticky eye' was examined bacteriologically throughout the year. The period of intensive investigation began in the latter part of June, by which time eleven cases of pemphigus had already occurred. At the outset, a careful review of the conditions in the nursery was made, and this did not reveal any gross breaches of technique by the staff. The nursery was somewhat overcrowded and understaffed, but it was not possible to effect any improvement.

Since the main reservoir of *Staph. aureus* is generally considered to be the nose (McFarlan, 1938; Gillespie, Devenish & Cowan, 1939; Williams, 1946) and the organisms at other sites are mainly derived

from this source, it was decided to concentrate our main efforts on nasal swabbing. At the first visit, nasal swabs of the staff, the mothers and the babies were collected. One week later the babies were re-swabbed. One week after this, daily swabbing of all infants in the nursery was begun, and continued for 5½ weeks, with one 5-day break in the middle which was due to pressure of other work. In addition, an initial swab was collected from each baby in the labour ward within a few minutes of birth. An attempt was made to secure nasal swabs on admission from all the mothers, but a few of the night admissions during busy periods were missed. The staff was swabbed five times at approximately weekly intervals.

Three months after the spontaneous cessation of the outbreak a control investigation was performed. One complete swabbing of the staff, and two swabbings of the babies at weekly intervals were carried out.

scribed by Wilson & Atkinson (1945) was followed except in one particular. Instead of spreading four drops of broth culture over the surface of the 0.2% glucose agar plate with a glass rod, about 1.0 ml. was pipetted on to the plate and distributed over the surface by rocking. In the last of four or five rocking movements, care was taken to see that the layer of liquid ran evenly over the entire plate. The excess of fluid was then removed from the tilted plate with the same pipette. We found that the films of bacterial growth obtained in this manner were more even than when a glass spreader was used.

The phage filtrates were supplied by Dr Allison, diluted to the highest dilution that gave confluent lysis with the corresponding propagating strain. Twenty-four such filtrates were used in each test.

Results of bacteriophage typing. Of the 210 strains examined, 136 (65%) were lysed by one or more of the phage filtrates. Twenty-one different 'patterns'

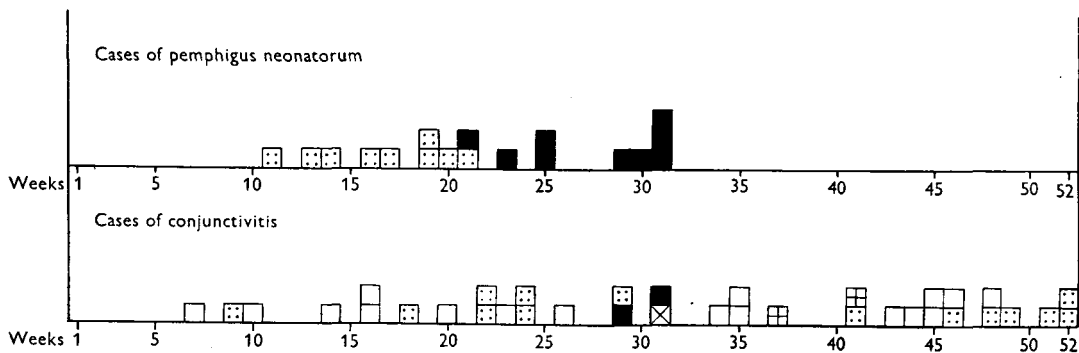


Fig. 1. The weekly occurrence of cases of pemphigus neonatorum and of conjunctivitis during 1946. □ *Staph. aureus* not isolated. ◻ *Staph. aureus* isolated, not typed. ■ *Staph. aureus* isolated, epidemic type (3A+). ⊠ *Staph. aureus* isolated, other types. ⊞ *Staph. aureus* isolated, untypable.

Technique. Material from bullae was collected on to dry sterile swabs after aseptic puncture of the overlying skin, which had been previously cleansed with sterile saline. Material from the eye and the nose was also collected on dry swabs. All swabs were inoculated on to 5% horse blood agar plates; these were examined after incubation at 37° C. for 18 hr. and again after a further 24 hr. at room temperature. Colonies resembling staphylococci were examined by the slide-coagulase method (Cadness-Graves, Williams, Harper & Miles, 1943) and by the tube test when necessary. After various modifications of the latter test had been tried, that of Fisk (1940), in which 0.1 ml. of broth culture was added to 1.0 ml. of a 1 in 10 dilution of human plasma, was finally adopted. All staphylococci giving a positive coagulase test were classified as *Staph. aureus*.

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of phage susceptibility were observed. Some of these were simple monospecific reactions with single phages, but others consisted of lysis of varying degree by six or seven filtrates. About one-half of the 'patterns' corresponded to the types described by Wilson & Atkinson (1945), but a number of other combinations were observed. For convenience the groups of strains characterized by the same pattern of phage susceptibility will be referred to as 'types'. It is not yet certain that such a classification has the same wide significance as that possessed by the Vi-phage types of *Salmonella typhi*. However, it may be assumed that strains of *Staph. aureus* which behave in an identical fashion when treated with a range of phage preparations, if collected from a single community within a relatively short time, are related to one another and have been derived from the same source.

THE BACTERIOLOGY OF THE
INFANT LESIONS

Pemphigus neonatorum

Staph. aureus was isolated from the local lesion of all eighteen cases of pemphigus neonatorum. Strains from the last nine consecutive cases of the outbreak were preserved for phage typing; all belonged to the same type (3A+), which will be referred to henceforth as the 'epidemic type'. Four out of five of the cases in which daily nasal swabbing had been carried out since birth were found to have been harbouring organisms of the epidemic type in their noses for some time before the occurrence of the local lesion. The intervals between first isolation from the nose and the development of the lesion were 2, 3, 3 and 11 days respectively. In the fifth case, nasal swabs were examined daily for 18 days and all were negative, although pemphigus occurred on the 12th day. In no case had the epidemic type of *Staph. aureus* been isolated from the nose of the mother of any of these infants on admission.

Of the thirty-six recorded cases of 'sticky eye', at least half were quite trivial and might have gone unrecorded but for the vigilance of the nursing staff. Bacteriological results were irregular. From thirty-six swabs, *Staph. aureus* was isolated nineteen times, *Staph. albus* seventeen times, organisms of the coliform group six times, viridans streptococci and diphtheroids each three times and pneumococci twice. In sixteen cases more than one kind of organism was isolated. Six of the swabs were sterile.

Three of the strains of *Staph. aureus* isolated from eye swabs during the pemphigus outbreak were available for phage typing. Two belonged to the epidemic type and one to another type (6/47+). In all three cases the same type of organism had appeared in the nose some days before the development of the 'sticky eye'. The mothers of the two cases infected with the epidemic type did not have the organism in their swabs on admission. However, the mother of the infant from whose eye the 6/47+ organism was isolated had the same type in her nose on admission. A routine vaginal swab collected during an attack of mild puerperal pyrexia also yielded a heavy growth of the same type.

Three strains of *Staph. aureus* from cases of 'sticky eye' that occurred in the month following the cessation of the pemphigus outbreak were untypable.

STAPHYLOCOCCUS AUREUS
IN NASAL SWABS

The Staff

Nasal swabs from the staff were collected on five occasions during the latter half of the outbreak. On the first occasion several persons were missed, but

subsequently a specimen was obtained from every-one working in the department. A sixth swabbing was carried out 3 months after the last case of pemphigus had occurred. One or more swabs were obtained from thirty persons; strains of *Staph. aureus* were isolated from twenty of these. The results are shown in detail in Fig. 2. *Staph. aureus* was obtained from about half of the staff in the first two swabbings. Later on, the proportion was rather less; this may have been due to the application of penicillin locally. Regular nasal spraying of the whole staff was first tried between 2 and 9 July. A solution containing 1000 units/ml. was sprayed into each nostril from an atomizer twice daily for 1 week. The result of swabbing 24 hr. after the last dose showed that it had been ineffective. Three carriers persisted, two had become negative, and three fresh ones had appeared. Later (26 July to 1 August) a solution containing 20,000 units/ml. was applied every 3 hr. throughout the working day for 1 week. The results on this occasion were doubtful, since one carrier persisted, two became negative and one new one appeared.

During the first five swabbings various phage types were present, and successive isolations from the same person were always of the same type. The epidemic type was isolated once from each of three members of the staff. In the first swabbing, two of the midwives were infected with it, but 1 week later both were negative. One of the two remained in the unit for the whole of the period and every subsequent swab was negative. The organism was isolated from a third nurse on one occasion later. Thereafter the type was not found among the staff, although cases of pemphigus continued to occur for a further 4 weeks.

The result of the last swabbing 3 months later showed that a considerable change had taken place. Of the staff still present in the unit who had had positive swabs previously, only one was harbouring organisms of the same type, and one other gave a growth of untypable organisms on both occasions. In three cases there had been a change of type. The epidemic type was not encountered.

The Mothers

Nasal swabs collected from 104 mothers on admission to the unit were examined; *Staph. aureus* was obtained from twenty-nine. Of these strains, eighteen were untypable; the remaining eleven fell into nine different phage types. The epidemic type was not represented. In general there was very little relation between the type present in the mother's nose and that subsequently isolated from her infant. On one occasion which has already been mentioned, the same type was obtained from the mother's nose and vagina, and her infant's nose and conjunctival sac, but this was an isolated occurrence.

The Infants

Six hundred and thirteen nasal swabs were collected from the infants during the latter part of the epidemic, mostly from daily swabbing of the whole nursery.

The swabs collected in the labour ward from ninety-six newly born infants were in most cases

haemolytic streptococci. On one occasion only, a strain of *Staph. aureus* was obtained.

The appearance of *Staph. aureus* during the first week after birth was in most cases sudden, a negative culture being followed next day by a heavy pure growth. Swabs from the infant carriers usually gave a much more profuse growth than those from the average adult carrier.

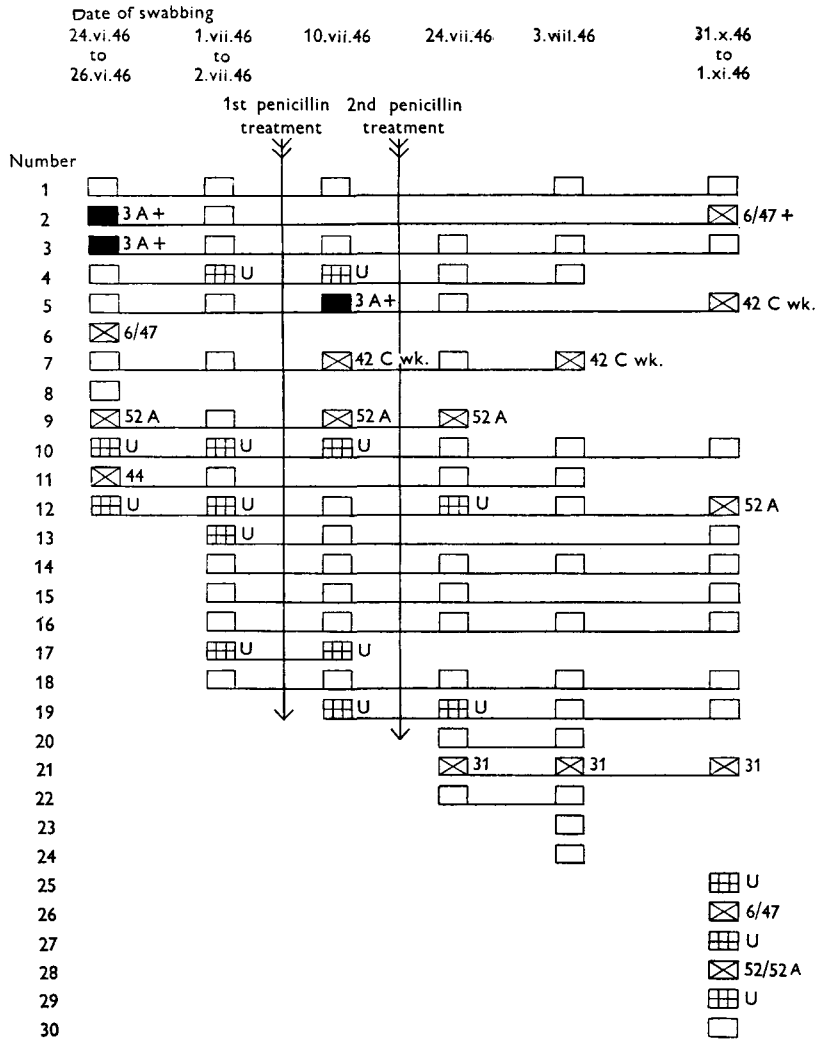


Fig. 2. Nasal carriage of *Staph. aureus* by the staff. ■ *Staph. aureus*, epidemic type (3A+). X *Staph. aureus*, other types (numbers refer to phage types). ▤ *Staph. aureus*, untypable. □ *Staph. aureus*, not isolated.

sterile. A few yielded a scanty growth of *Staph. albus*, other saprophytic cocci or coliform organisms. One gave a heavy growth of haemolytic streptococci of Group B, which persisted until the 8th day after birth. Subsequent investigation showed that the mother was a heavy vaginal carrier of Group B

Staph. aureus was isolated from 210 of the 613 swabs (34%). This relatively low percentage was due to the preponderance of swabs from infants in the first few days of life, caused by the policy of evacuation to the Maternity Annexe. The distribution according to age, shown in Table 1, indicates that the

percentage of positives rose steadily during the first few days after birth, reaching 50% at the end of the first week, and thereafter fluctuating between 60 and 80%.

Repetition of the swabbing 3 months after the end of the epidemic showed that *Staph. aureus* was still quite as prevalent in the infants' noses. Positive cultures were obtained from twenty-four of thirty-two swabs.

Of the 210 strains obtained, 102 were selected for phage typing. These included as far as possible (1) the organisms from the first positive swab from each

half of the positive cultures, and only one colony from each of the original plates was tested.

A clearer picture of the situation is given by Table 2, which shows the distribution of phage types in the weekly 'cross-sections' of the nursery population. It will be seen that on all occasions the epidemic type was present, and that on all but one it was the predominant type. The exception followed an attempt to reduce the sources of infection by the removal of as many as possible of the older infants to the Maternity Annexe. One persistent carrier of what was subsequently identified as the epidemic type was

Table 1. *Proportion of infants' nasal swabs positive for Staph. aureus at various ages*

	Age of infants (days)															Total	
	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15-		30+
No. positive	1	7	16	13	13	18	17	22	19	15	13	8	3	2	37	6	210
No. negative	95	76	48	40	34	24	22	16	15	9	7	4	2	3	8	0	403
Total	96	83	64	53	47	42	39	38	34	24	20	12	5	5	45	6	613

Table 2. *Prevalence of Staph. aureus and distribution of phage types in nasal swabs of 'cross-sections' of the nursery population in 1946 (infants only)*

Date ...	Latter part of epidemic							Non-epidemic period	
	24. vi.	1. vii.	8. vii.	16. vii.	23. vii.	31. vii.	7. viii.	29. x.	6. xi.
No. of infants in nursery	20	15	13	25	16	20	23	14	21
Number positive nasal swabs	12	7	2	8	5	7	11	6	18
Distribution of phage types									
Epidemic	7	6	1	6	4	4	9	0	0
6/47+	0	0	0	1	0	0	0	2	4
3B	1	0	0	0	0	0	0	0	0
29	1	0	0	0	0	0	0	0	0
3B/3C	0	0	0	0	0	1	1	0	0
52A	0	0	0	0	0	0	0	1	3
6+	0	0	0	0	0	0	0	0	3
47A	0	0	0	0	0	0	0	0	1
52	0	0	0	0	0	0	0	0	1
Other types	0	0	0	0	0	0	0	0	1
Untypable	3	1	1	1	1	2	1	3	5

infant, and (2) others selected so as to provide a series of 'cross-sections' of the types present at approximately weekly intervals. Seventy-seven of the strains were found to be typable and of these sixty-six belonged to the epidemic type.

In all, *Staph. aureus* had been isolated from fifty-four infants, and of these thirty-eight were carrying the epidemic type. Organisms of other types were isolated from five, and untypable organisms from a further eighteen infants. On seven occasions, two different types were identified from successive swabs of the same infant. This is probably an underestimate of the prevalence of the epidemic type, since phage typing was carried out on organisms from less than

retained, and a week later the organism had again become predominant.

The distribution of types among the strains obtained 3 months later was quite different. Six different phage types were identified, in addition to untypable strains, and none was markedly predominant. Two of the more common, however, were identical with types present among the nursing staff at the same time. The epidemic type was not found.

DISCUSSION

Since the introduction of slide agglutination (Cowan, 1939) and phage typing (Wilson & Atkinson,

1945) as means of classifying strains of *Staph. aureus*, a number of investigations into the epidemiology of pemphigus neonatorum have been reported (Elliott, Gillespie & Holland, 1941; Hobbs, 1944; Allison & Hobbs, 1947; Williams, Sims-Roberts & Cook, 1947). In each case, the epidemic type of organism was isolated from one or more of the nursing staff, usually a person in intimate contact with the infants. Although the possibility of spread from infant to infant was recognized by some of these authors, the main emphasis was on the adult as the immediate source of infection. Allison & Hobbs (1947) found a high carrier rate of the epidemic type among the staff at the beginning of two of their outbreaks and suggested that a 'build-up' of infection among the adults might be a necessary preliminary to the occurrence of an outbreak among the infants.

In the present investigation, the mothers were swabbed on admission to the unit, and none was found to be carrying the epidemic type of organism. This agreed with the findings of others (Duncan & Walker, 1942; Hobbs, 1944; Allison & Hobbs, 1947), who consider that the mother is not an important source of infection. Occasionally, spread from mother to infant undoubtedly does occur, and an example involving a different phage type of *Staph. aureus* was observed by us, but it is probably not common.

The nursing staff was swabbed repeatedly during the latter part of the outbreak, and no persistent carrier of the epidemic type was found. The organism was isolated on a single occasion from each of three nurses. These transient carriers were all working in a heavily infected environment, and may have been infected from the infants. Members of the staff who were carriers of other phage types showed a greater tendency to persistence over a 6-week period. The most significant fact, however, was that cases of pemphigus continued to occur in the nursery during a period of several weeks when no nasal carrier of the epidemic type could be found among the staff.

The epidemic type was widely distributed among the infants during the whole of the latter part of the epidemic. It was the type most commonly isolated from nasal swabs, and was usually present in profuse pure culture. No attempt was made to assess the distribution of the organism in other parts of the body, but it is probable that it was very widespread (Duncan & Walker, 1942; Knott & Blaikley, 1944). In similar circumstances, Allison & Hobbs (1947) have shown that the epidemic type could be isolated from the infants' clothes and bedding.

The ultimate source of the organisms responsible for pemphigus neonatorum must presumably be the nasal passages of an adult. In some outbreaks, and in isolated cases occurring in domiciliary practice, direct transference from adult to infant probably

takes place. However, in the special conditions of an overcrowded nursery, the evidence indicates that a type of *Staph. aureus* can be propagated from 'generation' to 'generation' of infants, giving rise to a high carrier-rate and a succession of clinical skin lesions. The organism is often present in eye swabs of cases of conjunctivitis occurring at the same time, though it is not certain that they all represent primary staphylococcal infections.

The epidemic strain of *Staph. aureus* is only one of a number with which the newborn infant comes into contact, since the staff and the mothers usually harbour a variety of different types. During a period of prevalence of pemphigus neonatorum, however, the epidemic type appears to possess a high degree of transmissibility by virtue of which it becomes and remains the predominant type in the infant community. In non-epidemic times, the flora of the nursery tends to be more heterogeneous.

There is a wide variety of possible paths of spread of *Staph. aureus* from one individual to another, and an efficient nursery technique is designed to prevent spread by all of them. However, present standards of accommodation and staffing make the carrying out of such a technique quite impracticable in many institutions. Thus the periodic occurrence of outbreaks of staphylococcal infection is inevitable. Measures to reduce the prevalent overcrowding are of the utmost importance in their prevention. Where shortage of accommodation makes this difficult, the alternative of placing the infants' cots at the foot of the mothers' beds may have to be considered. There is little doubt that the abolition of large nurseries in maternity departments would greatly reduce the number of outbreaks of infection.

It is often difficult to decide on a course of action when cases of pemphigus neonatorum occur. Outbreaks of staphylococcal infection among infants are very variable in severity and course. While some, such as the one described in this article, consist of mild cutaneous lesions, others also include highly fatal cases of staphylococcal pneumonia and generalized infection. Moreover, sporadic cases occur from time to time and it is often difficult to be sure when an outbreak is starting.

Frequent closure of a maternity unit causes great hardship to the mothers and should be avoided if possible. If the unit is of modern design with a number of small wards it is easier to control the spread of infection and closure should not be necessary unless the clinical type is severe or the number of cases very large. In an old-fashioned badly designed unit it may be necessary eventually to advise closure in order to control outbreaks of a mild clinical type, but less extreme measures may be tried if the cases are few and infrequent.

The occurrence of even a single case should lead to a careful review of the nursing technique and an

attempt to reduce the size of the infant population. The affected child and its mother should be removed from the unit, either to their home or to the Infectious Diseases' Hospital. If further cases occur, all babies born after a certain date may be kept out of the nursery, the cots being placed by their mothers' beds. This is often difficult to arrange because of the absence of adequate facilities for bathing the babies outside the nursery.

When an outbreak continues despite the application of such mild remedies the question of closure of the entire unit must be considered. If it is decided to carry on, more radical preventive measures designed to deal simultaneously with the two possible sources of infection, namely the staff and the 'contact' infants, should be employed wherever possible. These should begin with the closure of the nursery to new admissions, and the setting up of a new nursery with an entirely fresh staff consisting of persons who have not worked in the unit recently. All infants born subsequently should be placed in the new nursery. As soon as the old nursery can be emptied by a process of accelerated discharge, it should be thoroughly cleaned and disinfected. The occupants of the new nursery can then be moved into it with their own staff. In the meantime, bacteriological investigations to determine the infecting type and its distribution among the 'old' nursery staff can be carried out. Those who have been free from the epidemic type on several successive occasions after their last contact with potentially infected infants can return to the nursery and replace the temporary staff. Success depends upon complete absence of contact between

the old and new nurseries. This must include separate kitchens, and the efficient sterilization of all towels, clothes, napkins and blankets before they are sent to the laundry. The application of such measures will be beyond the resources of many hospitals owing to lack of staff or accommodation, but in favourable circumstances it may be possible to avoid the disorganization and hardship that occur when a maternity unit is closed at short notice.

SUMMARY

An outbreak of eighteen cases of pemphigus neonatorum in a maternity department is described.

Strains of *Staph. aureus* isolated from the infants, the mothers and the staff during several weeks of intensive investigations were classified by phage typing.

The findings indicated that, during the latter part of the outbreak at least, the adults were not the source of infection.

There was evidence of wide dissemination of the epidemic strain of *Staph. aureus* among the healthy infants in the nursery. It is suggested that the main path of infection was from infant to infant.

Methods of controlling established outbreaks are discussed.

We wish to express our gratitude to Dr V. D. Allison for much help and advice and for the supply of phage filtrates, and to Mr J. R. E. James for permission to investigate his cases.

REFERENCES

- ALLISON, V. D. & HOBBS, BETTY C. (1947). *Brit. Med. J.* **2**, 1.
- CADNESS-GRAVES, B., WILLIAMS, R., HARPER, G. J. & MILES, A. A. (1943). *Lancet*, **1**, 736.
- CHAPMAN, G. H. (1945). *J. Bact.* **50**, 201.
- COWAN, S. T. (1939). *J. Path. Bact.* **48**, 169.
- DUNCAN, J. T. & WALKER, JACQUELINE (1942). *J. Hyg., Camb.*, **42**, 474.
- ELLIOTT, S. D., GILLESPIE, E. H. & HOLLAND, E. (1941). *Lancet*, **1**, 169.
- FISK, A. (1940). *Brit. J. Exp. Path.* **21**, 311.
- GILLESPIE, E. H., DEVENISH, E. A. & COWAN, S. T. (1939). *Lancet*, **2**, 870.
- HOBBS, BETTY C. (1944). *Mon. Bull. Min. Hlth Publ. Hlth Lab. Serv.* **3**, 11.
- KNOTT, F. A. & BLAKLEY, J. B. (1944). *J. Obstet. Gynaec.* **51**, 386.
- McFARLAN, A. M. (1938). *Brit. Med. J.* **2**, 939.
- WILLIAMS, G. C., SIMS-ROBERTS, CAROL & COOK, G. T. (1947). *Mon. Bull. Min. Hlth Publ. Hlth Lab. Serv.* **6**, 13.
- WILLIAMS, R. E. O. (1946). *J. Path. Bact.* **58**, 259.
- WILSON, G. S. & ATKINSON, J. D. (1945). *Lancet*, **1**, 647.

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