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A five year outbreak of methicillin-susceptible *Staphylococcus aureus* phage type 53,85 in a regional neonatal unit

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SUMMARY

We identified a 5-year outbreak of a methicillin-susceptible *Staphylococcus aureus* (MSSA) strain, affecting 202 babies on a neonatal unit, by routine weekly phage typing all *S. aureus* isolates. Multiple staged control measures including strict emphasis on hand hygiene, environmental and staff surveillance sampling, and application of topical hexachlorophane powder failed to end the outbreak. *S. aureus* PT 53,85 (SA5385) was found on opened packs of Stomahesive®, used as a neonatal skin protectant. Only following the implementation of aseptic handling of Stomahesive, and the use of topical mupirocin for staff nasal carriers of SA5385, and for babies colonized or infected with *S. aureus*, did the isolation rate of SA5385 decline. DNA fingerprinting indicated that $\geqslant 95\%$ of SA5385 isolates were clonal. *In vitro* death rates of SA5385 on Stomahesive with human serum were significantly lower than on Stomahesive alone ($P = 0{\cdot}04$), and on cotton sheet with serum ($P = 0{\cdot}04$), highlighting the potential of this material as a survival niche. Phage typing remains a valuable, inexpensive and simple method for monitoring nosocomial MSSA infection.

INTRODUCTION

Neonatal units provide ideal environments for *Staphylococcus aureus* to persist as a nosocomial pathogen. Most of the infants are of low birth weight, debilitated and subjected to many invasive procedures, including the insertion of intravascular catheters. Babies on neonatal units also develop commensal flora which differ from those not managed in intensive care, possibly influencing their colonization by potentially pathogenic bacteria [1, 2]. *S. aureus* has long been recognized as a major hospital-acquired pathogen of neonates [3–5]. The umbilicus is a prime site of colonization, and umbilical colonization and neonatal infection are closely related [3–5]. Hand-borne spread is the predominant means of staphylococcal transmission in neonatal units [6, 7]. In many outbreaks of methicillin-resistant and methicillin-susceptible *S. aureus* (MRSA, MSSA), employment of extra staff has brought about a reduction in rates of infection [8–10]. In particular, the employment of an infection control nurse often improves the situation by drawing attention to and implementing infection control measures [10]. *S. aureus* survival within the hospital environment is well documented [11–13], and some epidemic strains can remain viable for longer on cotton lint than other strains [14]. The mechanisms of enhanced survival are poorly understood, but resistance to desiccation [13, 15], adherence [16], and the ability to survive on human skin [15–17] have been implicated.

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Recently, much emphasis has been placed on outbreaks caused by MRSA [18–21]. The spread of MSSA has received less attention, largely because these bacteria do not have readily identifiable antibiotic resistance markers, and many laboratories have abandoned routine monitoring methods such as phage type. We have continued to monitor and phage type MSSA isolates, and highlight the value of such surveillance. Routine phage typing enabled us first to identify and then monitor the control of a 5-year outbreak of *S. aureus* PT 53,85 (SA5385) in our regional neonatal unit (subsequently confirmed by DNA fingerprinting). Secondly, we emphasize the epidemic potential of this MSSA strain and the extensive measures required for its control. Thirdly, we report the potential environmental niche provided by Stomahesive® (Squibb, UK), which is used as a neonatal skin protectant. *In vitro* staphylococcal desiccation experiments confirmed the survival of bacteria on Stomahesive, and successful control of the outbreak was only achieved once aseptic handling procedures for this material were adopted.

METHODS

Overview of the outbreak

Retrospective analysis of PT results (performed weekly since 1980s) showed the outbreak of SA5385 began on the neonatal unit in September 1992, when it was isolated from eye swabs taken from twin baby girls with sticky eyes on the special care baby unit. The outbreak was centred on the neonatal unit (145 new isolates), but 92 SA5385 isolates were also recovered from babies on two post-natal and paediatric intensive care wards (usually after transfer from the neonatal unit), and rarely from elsewhere (total $\leqslant 3$ isolates per annum). Data presented pertain primarily to the neonatal unit, which has about 900 admissions per year (including 175 neonates weighing < 1500 g and/or < 31 weeks gestation, 400 ventilated babies and 300 surgical cases) and consists of adjoining intensive care (10 cots, including 2 in a side room), special care (20 cots in 3 cuticles and 1 side room) and surgical (10 cots units, including 2 side rooms) units. Figure 1 depicts the outbreak (but excludes multiple patient isolates and those obtained from screening specimens) and demonstrates peaks of new isolates of SA5385 in 1995 and mid-1996. It was often unclear whether isolation of SA5385 represented colonization or infection. However, 28% of SA5385 isolates were recovered from normally sterile sites (blood, CSF, intravascular catheter tips, joint fluids, pleural aspirates), particularly in 1994–5 (60% of invasive isolates); the remainder were isolated from non-sterile sites (e.g. wound, skin, eye and nasopharyngeal swabs, urine and sputum) indicating colonization (with or without infection). Infections caused by SA5385 ranged from conjunctivitis to septicaemia and osteomyelitis; in two cases the strain was isolated from peritoneal swabs from infants with necrotizing enterocolitis. The two most common clinical conditions were conjunctivitis and respiratory compromise (apnoea, decreased oxygen saturation, increased tracheal secretions, and, occasionally, consolidation on chest X-ray). Seven sporadic cases of MRSA infection/colonization (including EMRSA 15/16) were seen on the neonatal unit during the outbreak period. Control measures resulted in a marked reduction in new SA5385 isolates in the latter half of 1996. Data were analysed using Microsoft Excel 5.0 software.

In vitro studies

Bacterial isolates

Staphylococci were isolated from sterile and non-sterile sites from babies on neonatal wards (using 5% blood agar and CLED agar; Unipath, Basingstoke, UK), and identified as *S. aureus* using Staphyslide (BioMerieux, Basingstoke, UK) and DNAse testing. Phage typing [22] was carried out using $\times 100$ routine test solution of 23 international phages [23] on all *S. aureus* isolates each week. Environmental testing was carried out using blood agar settle plates, and saline moistened, cotton wool swabs to sample 10×10 cm areas followed by inoculation onto blood agar. All SA5385 isolates were stored at -70 °C following phage typing. Forty non-consecutive, random, stored isolates were selected for pulse field gel electrophoresis of chromosomal DNA, plasmid profiling an antimicrobial susceptibility testing. For desiccation studies, 5 randomly selected SA5385 strains, and 15 non-PT 53,85 *S. aureus* isolates (5 each from healthy human volunteers, neonates and patients on other hospital wards) were used.

Pulsed field gel electrophoresis (PFGE)

Agarose blocks were prepared using modified manufacturer's instructions (BioRad, Hemel Hempstead, UK). Briefly, strains were incubated overnight in

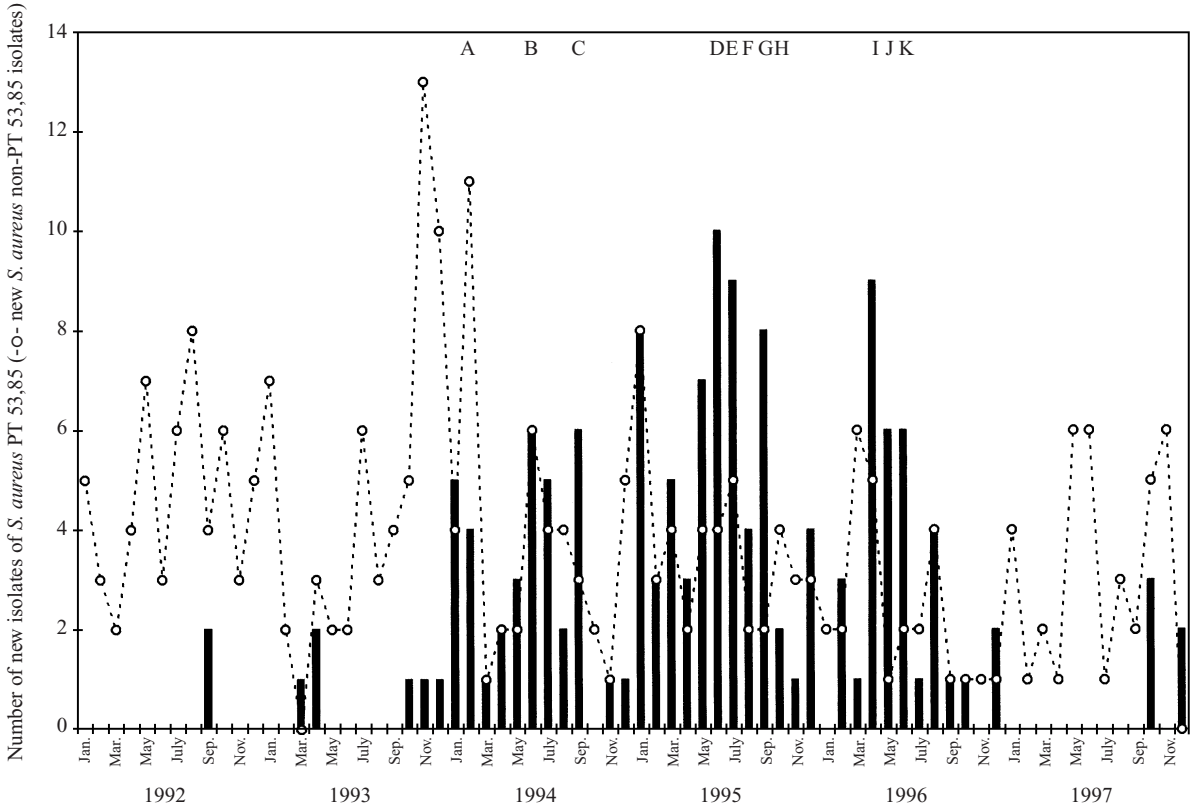

Fig. 1. Frequency histogram to show the outbreak of *S. aureus* PT 53,85 on the neonatal unit (new patient isolates) 1992–7. The dotted line (--○--) shows the numbers of other *S. aureus* isolates. The main intervention points, depicted by the letters, were as follows: A, staff and environmental screening, mupirocin for carriers; B, repeat nasal mupirocin for staff carriers plus topical Aquasept; C, routine topical hexachlorophane to umbilicus of neonatal unit babies post-bathing; D, measures in C extended to babies on post-natal wards; E, treatment of all staff with nasal mupirocin and topical Aquasept, plus thorough environmental cleaning; F, nasal mupirocin for patients carriers; G, repeat F plus cohorting of carriers; H, extensive staff and environmental screening; I, extensive surveillance exercise of neonatal unit procedures; J, Stomahesive implicated in outbreak, aseptic handling protocol introduced; K, empirical nasal mupirocin for babies from whom *S. aureus* isolated. See text for full details.

tryptone yeast extract broth (Oxoid) with 10% glycine. Following centrifugation of 1 ml aliquots at 12000 ***g*** for 10 min at 4 °C, the deposit was washed in 1 ml of buffer (10 mM Tris, 50 mM EDTA, 1 M NaCl) and then suspended in 0·5 ml buffer. The suspension was heated at 50 °C and then an equal volume of 1% low melting temperature agarose (Flowgen, Lichfield, UK) was added and poured into moulds. For each strain tested, two agarose blocks containing DNA were incubated in buffer containing 1 mg/ml lysozyme (Sigma, Poole, UK) and 200 μl/ml lysostaphin (Sigma) for 4 h at 37 °C, then washed and incubated overnight at 50 °C in 1 mg/ml proteinase K (Sigma). The blocks were then washed, and digested using 20 U of restriction endonuclease (*Sma*I; Helena Biosciences, Sunderland, UK) for 2 h. Electrophoresis was carried out using a CHEF–DR II system (Bio-Rad) at 14 °C with a constant voltage of 6 V cm^{-1} and pulse times of 45–90 sec for 8 h, 5–25 sec for 12 h. Gels were stained with 1 μl ml^{-1} ethidium bromide and photographed under u.v. light.

Plasmid analysis

Plasmid DNA was extracted from isolates using Wizard miniprep (Promega, Southampton, UK). Manufacturers' instructions were modified to include an incubation step with 2 mg/ml lysostaphin before lysis. Plasmid DNA was analysed by electrophoresis on 0·8% w/v agarose gels, which were then stained and photographed as for PFGE.

Antimicrobial susceptibility testing

Determination of the MICs of 8 antibiotics, 3 antiseptics and 2 DNA binding agents for 40 strains

was carried out by an agar dilution method (Isosensitest agar, Oxoid) and multipoint inoculation of 10^4 d.f.u./spot [24]. Tested compounds, obtained as pharmaceutical grade powders/solutions or from Sigma (breakpoint concentrations, mg/l), were acriflavine (32), amikacin (8), benzalkonium chloride (8), chloramphenicol (32), chlorhexidine (4), erythromycin (8), ethidium bromide (32), flucloxocallin (4), gentamicin (4), netilmicin (4), penicillin (0·25), triclosan (4), and trimethoprim (8) [24–26]. The control was *S. aureus* NCTC 6571.

Resistance to desiccation

It was hypothesized that contaminated Stomahesive® was a focus for SA5385 in the Neonatal Unit. To test the hypothesis, we compared *in vitro* survival rates of 20 *S. aureus* strains, including 5 SA5385, on Stomahesive® using a modified desiccation method [15]. Overnight cultures of each strain grown in 10 ml Brain Heart Infusion broth (Oxoid) were centrifuged, washed, and re-suspended in 4 ml phosphate buffered saline (PBS). Each suspension was divided into two 2 ml aliquots, and 1 ml of pooled human serum was added to one of these. Each sample volume was then made up to 5 ml with PBS. Aliquots (20 μl) from each of the two samples per strain were placed on five 30 mm squares of sterile cotton sheeting, and five 10 mm squares of Stomahesive®. Cotton squares were placed in individual sterile 10 cm diameter Petri dishes, and Stomahesive® squares were stored five to a dish. Covered Petri dishes were stored in darkness at ambient temperatures (22 °C) and humidity. Surviving bacteria were quantified on days 1, 7, 14, 21 and 71, by determining viable counts on squares following broth immersion and vortexing for 30 sec. Viable bacteria were enumerated by tenfold dilutions of broth from the vortexed squares, plated on blood agar by the spread technique. The death rate per day (K) was calculated as $K = 2{\cdot}3 \times 1/t(B_0 - B_t)$, where t is the drying time in days, $B_0 = \log_{10}$ count at time 0, $B_t = \log_{10}$ count at time t [13]. The significance of differences in K values was determined by Student's t test.

RESULTS

Infection control procedures

An outbreak meeting was first held in February 1994 following a peak of SA5385 isolates 2 months previously. Nasal swabs from 170 health carers yielded SA5385 from 4 nurses and 1 doctor who were given nasal mupirocin for 1 week. All were negative on repeat swabbing. Extensive environmental sampling was performed but no SA5385 positive sites were identified. Hand hygiene awareness on the neonatal unit was increased (teaching, demonstrations and hand impression plate result feedback). No staff attending the Caesarian section delivery of a positive baby were SA5385 nasal carriers (April 1994). New SA5385 isolates reduced after the first infection control measures (Fig. 1, A), but increased steadily over the next 5 months. Infection control measures were re-iterated, followed by another decline in SA5385 isolates.

In June/July 1994, 45 staff nasal swabs (26%) grew *S. aureus* including 6 (4%) SA5385 (Fig. 1, B). Carriers were treated and re-tested as before, but in addition Aquasept (triclosan 2% w/v; Seaton Healthcare, Oldham, UK) was used for bathing/showering. One staff member remained positive, but responded to a further course of nasal mupirocin. Environmental sampling did not yield any SA5385 isolates. From July 1994, hand hygiene products available on the unit were rationalized to Aquasept (triclosan 2% w/v) and Manusept (isopropyl alcohol 70% v/v, triclosan 0·5% w/v; Seaton Healthcare). A hand hygiene education programme was started and repeated every 6 months to maintain staff compliance. Babies admitted from other units were screened for SA5385, although none proved positive. A liaison nurse was identified in order to improve communication between ward staff and the ICT.

From September 1994, routine application of hexachlorophane 0·33% powder (Ster-Zac, Hough Hoseason, Manchester, UK) to the cord and umbilical area after bathing was introduced for all babies on the neonatal unit (Fig. 1, C), and this had a profound effect (only two new SA5385 isolates over the next 3 months). This policy was extended to the post-natal wards in June 1995 (Fig. 1, D), at which time extensive environmental sampling was undertaken. SA5385 was recovered from three settle plates in different rooms, a cot, a baby warmer and a filing drawer. The monthly incidence of SA5385 isolates was now at the highest level recorded. The ICT considered either closure of the neonatal unit, or extensive reinforcement of infection control measures. The unit is a regional referral centre and thus the effects of closure would potentially be dramatic. The second option was therefore adopted. Staff rotation in the unit was

Table 1. *Results of hand impression plate testing* (*July 1995*)

	Post-natal ward	Post-natal and transitional care ward	Neonatal unit
Number of staff tested	22	30	49
Number positive for *S. aureus*	4	7	9
Number of positive for *S. aureus* PT 53,85	0	3	8
Number positive before handwashing	1	3	6
Number positive before and after handwashing	3	4	3

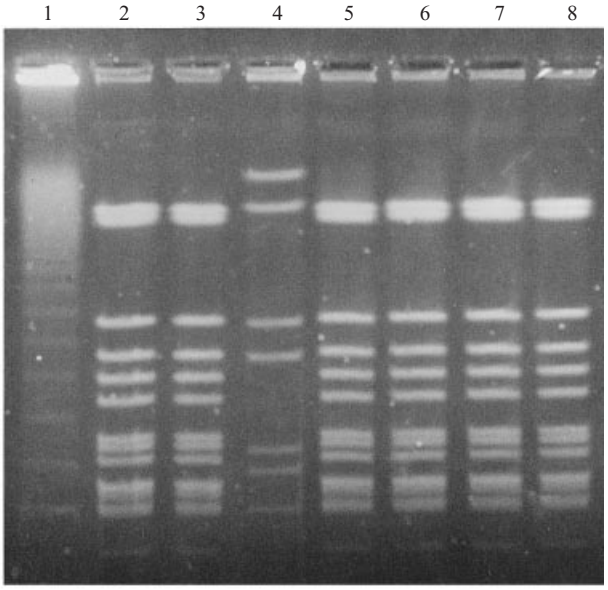

Fig. 2. Chromosomal DNA fingerprints (PFGE profiles following *Sma* I digestion) of *S. aureus* PT 53,85 clinical isolates (lanes 2–3, 5–8) and a non-typable *S. aureus* clinical isolate (lane 4). All isolates were recovered from sterile sites of babies on the neonatal unit. Lane 1 contains λ DNA ladder.

minimized, and all staff were treated with nasal mupirocin for 5 days, and Aquasept used daily for 1 week for bathing, showering and hair washing. Thorough environmental cleaning of the unit was carried out during and after staff treatment (Fig. 1, E). Hand impression plate cultures from neonatal unit and post-natal ward staff, indicates the presence of SA5385 on washed hands (Table 1; the outbreak strain was recovered from the hands of 8.49 neonatal unit staff, and in 3 of these was not removed post-washing), and therefore hand washing protocols for were re-emphasized and included a minimum wash for 2 min at the start of work. All infants with SA5385 nasal colonization were treated with mupirocin (Fig. 1, F). Hexachlorophane powder was used routinely on all babies at every nappy change (umbilicus, groin and axillae) on neonatal and post-natal wards. Laundered clothing was sampled for SA5385 but none was positive.

In September 1995 (Fig. 1, G) all babies on neonatal and post-natal wards had nose, perineal, umbilical, and skin lesion swabs taken. Eight babies colonised by SA5385 were cohort nursed in view of limited side room facilities. Babies were not transferred from the unit until colonization by SA5385 had been eradicated. Following reports of non-compliance, the hand hygiene protocol was reiterated (Fig. 1, H). Staff hand impression plates and nasal and skin lesion swabs grew 9 *S. aureus* isolates, but no SA5385. None of 95 environmental samples was *S. aureus* positive. New isolates were now at the lowest level since the outbreak began, but then rose rapidly in April 1996, prompting an extensive review of neonatal unit procedures by the ICT (Fig. 1, I).

In June 1996 SA5385 was isolated from a used piece of Stomahesive® (Squibb), and then from two pieces of pre-cut (but unused) material and the used scissors. Stomahesive® is supplied as a sterile product in 10×10 cm sheets, and staff had been cutting pieces as required to fit on neonates' faces, to protect against shearing forces occurring when conventional adhesive tape is removed. Aseptic precautions had not been observed routinely, and after sectioning remaining Stomahesive® was stored loosely in its original packaging in a drawer, or in an emergency tray on the open ward. A protocol was implemented for the aseptic handling of Stomahesive® (using gloves and sterile scissors) and storage in capped, sterile containers (Fig. 1, J). As there was a delay in obtaining phage typing results (performed weekly), nasal mupirocin was henceforth given empirically to babies whose clinical specimens yielded *S. aureus* (Fig. 1, K).

Table 2. *Comparison of* in vitro *death rates* (*values*) *of 20* S. aureus *strains on Stomahesive* (*S*) *and cotton sheet* (*C*) *in the presence* (+*hs*) *and absence* (−*hs*) *of human serum*

	C+hs	C−hs	S+hs	S−hs	C+hs	S+hs	C−hs	S−hs
Mean (S.D.) *K* value	0·22 (0·02)	0·19 (0·02)	0·13 (0·01)	0·22 (0·01)	0·22 (0·02)	0·13 (0·01)	0·19 (0·02)	0·22 (0·01)
P value*		0·65		0·04		0·04		0·68

* Two-tailed *t*-test.

A marked reduction in new SA5385 isolates followed in the latter half of 1996. SA5385 was not isolated in the first 9 months of 1997 but was then cultured from five neonates. Four babies in cots adjacent to the new cases were nasal carriers and treated with mupirocin. Infection control protocols for handling of Stomahesive®, use of alcohol hand rub, Aquasept bathing, and use of shared items were re-emphasized. There were no further SA5385 isolates up until the end of March 1998. There was a 68% decrease in the incidence of SA5385 during the 12 months after this change in protocol (15 isolates) compared with the 12 months before (47 isolates). The incidence of non-PT 53,85 *S. aureus* isolates was approximately stable during the outbreak (Fig. 1).

Staffing levels on the neonatal unit

Patient care hours (PCH) are the theoretical number of nursing hours required to accommodate the workload [10, 27, 28]. Nursing care hours (NCH) are the actual number of nursing hours worked. The greatest differences between PCH and NCH occurred in October 1993, May 1994, and March 1995. In respective months following these peaks, numbers of SA5385 isolates increased on the neonatal unit. In months when the PCH–NCH value was small (August 1994, September 1995), reduced numbers of new PT 53,85 isolates followed. However, linear regression analysis and Pearson's correlation coefficient indicated a non-significant relationship between the PCH–NCH values (for the current or preceding month) and the numbers of new SA5385 ($P \geqslant 0{\cdot}79$).

PFGE, plasmid analysis, antibiotic resistance profiles

PFGE profiles of 38/40 (95%) SA5385 isolates were indistinguishable (Fig. 2), with the remaining two strains closely related (three band difference) [29]. There were three plasmid profiles, differing by one or two bands. Isolates had very similar antimicrobial resistance profiles and 95% (38/40, with indistinguishable PFGE profile) were resistant to $\leqslant 4$ compounds. Only resistance to penicillin (36 strains), ethidium bromide (34), and acriflavine (34) was common. Three strains (with the common PFGE profile) were resistant to triclosan; these were isolated before and after institution of triclosan hand washing. None of the tested isolates was resistant to mupirocin.

Resistance to *S. aureus* to desiccation

All four groups of strains tested had similar trends in survival rates. There were large decreases in viable counts of most strains by day 7; the bacterial count declined more slowly up to days 21–71. There was no significant difference in bacterial survival rates between any of the *S. aureus* groups (*t*-test, $P > 0{\cdot}05$). There was also no significance between survival rates on the cotton sheet with and without serum, or between the cotton sheet without serum and the Stomahesive® without serum. However, survival rates on Stomahesive® with serum were significantly higher than on Stomahesive® alone ($P = 0{\cdot}04$), and on cotton sheet with serum ($P = 0{\cdot}04$) (Table 2).

DISCUSSION

The 5-year outbreak of SA5385 was centred on neonatal and postnatal wards, and only rare, sporadic isolates from patents elsewhere had similar phage types to the endemic strain. For example, a 2-year-old child with endotracheal tube secretions colonized by SA5385 was on the adjacent paediatric intensive care unit for 10 months and yet spread to other unit children was not seen. We cannot be certain of the true number of infected as opposed to colonized babies, but 61 isolates (from different babies) were recovered from specimens obtained from sterile sites. Phage typing all clinical *S. aureus* isolates enabled us to identify and then monitor the outbreak strain. DNA fingerprinting of 40 randomly selected SA5385

isolates confirmed that the outbreak was due to a distinct clone. While genotypic methods have become more common, phage typing remains a simple, inexpensive method for fingerprinting *S. aureus*, and is well suited to the examination of large numbers of strains, unlike the former techniques. Alert organism-based surveillance may have detected this outbreak, but it was not until 2 years after the outbreak began that the total number of *S. aureus* isolates on the unit increased markedly (Fig. 1).

There is currently much debate about control measures for MRSA [18–21] but we are concerned that there may be unrecognized spread of MSSA. We can find no other reports of SA5385 outbreaks, but this may reflect the relative rarity of routine *S. aureus* phage typing. Whilst some (epidemic) MRSA clearly have a propensity to spread, there are likewise many examples of MSSA with similar survival advantages [7–11]. Interestingly, during the SA5385 outbreak, seven sporadic MRSA isolates (including EMRSA 15/16) were identified on the neonatal unit. These were successfully contained using measures which were unsuccessful in preventing the spread of SA5385. Also, the incidence of *S. aureus* isolates other than PT 53,85 remained approximately stable during the outbreak period (Fig. 1), so emphasising the epidemic potential of this particular MSSA strain.

Outbreak control measures were hindered by the long stay of some colonized babies, limited isolation facilities, and movement of staff and babies within the unit. Marked reductions in new SA5385 isolates occurred (Fig. 1, interventions F and G) after limiting intra-unit transfer and introduction of cohorting or barrier nursing of infected/colonised babies. Transfer within the unit may facilitate efficient use of specialist cots and nursing care, but excessive movement can be counter-productive, because of the impact on infection control measures [30, 31]. We were unable to confirm staff shortages as a significant factor in this outbreak. Staphylococcal outbreaks have been linked to staff shortages and indeed successfully controlled by remedying this issue [8–10]. Overcrowding on neonatal units has also been associated with cross-infection [9]. However, the fact that we were eventually able to control the outbreak, without reducing numbers of babies on the unit, implies this issue was not a major factor. SA5385 was particularly refractory to the extensive infection control measures which were implemented. We suspected a survival niche for the strain but were unable to confirm sites such as monitors or ventilators [11, 32]. Antimicrobial resistance was not a factor in the persistence of SA5385, as determined by review of pharmacy data for the four most commonly prescribed antibiotics on the neonatal unit, ampicillin, gentamicin, aztreonam and vancomycin (data not shown). Antibiotic policy and use remained constant during the outbreak. Hexachlorophane powder as part of an umbilical care regimen is effective [7, 33], and was initially so in this outbreak. However, maximal effectiveness is only likely to be achieved when used with other infection control measures. Hand washing was the most emphasized control measure, and was transiently effective at reducing the incidence of new SA5385 isolates, but periodic audit indicated that staff non-compliance occurred. Haley noted that recruitment of an ICN from neonatal unit staff was beneficial in obtaining compliance with hand washing protocols [10]. The outbreak prompted us to ensure that new staff on the unit received formal infection control teaching in their induction scheme. Staff screening for staphylococcal carriage was limited to nose and hands only. When staff carried of SA5385 was detected we used a whole body surface decontamination regimen which would be expected to markedly reduce bacterial density at other sites. Also, given the poor yield of the endemic strain from repeated nose/hand staff sampling exercises, it is unlikely that extended screening would have yielded many further positive individuals. Elsewhere, the yield of clinically significant MRSA isolates from staff specimens is often extremely low [34, 35].

The only intervention producing a sustained response was the combination of aseptic handling of Stomahesive, and the empirical use of nasal mupirocin for babies from whom *S. aureus* was isolated. These protocols were started simultaneously, although nasal mupirocin was not used for babies with *S. aureus* in respiratory secretions whilst endotracheal tubes remained *in situ*, as we considered that nasal eradication would be unlikely. We therefore believe that the main factor which reduced the spread of SA5385 was the aseptic handling of Stomahesive, so removing a hitherto unrecognized niche for staphylococci. We tried to confirm Stomahesive as source of SA5385 by sampling further used pieces, but these often became detached from babies' faces after several days. We felt that we had to intervene on the basis of the evidence we had, rather than conduct a controlled observation period. Mupirocin nasal cream appeared to be effective in eradicating nasal carriage of SA5385, although in September 1995, anecdotal evidence came

to light regarding non-compliance of staff in the use of mupirocin cream and hand washing. This may explain why the earlier success of the mupirocin eradication programme was not repeated in 1995, when isolation rates increased sharply. Mupirocin resistance was not detected during the outbreak [36]. It is usual practice to adopt staged infection control measures. It is possible that there was a cumulative benefit from initial control measures, implementation of aseptic handling of Stomahesive, and empirical use of nasal mupirocin. Hence, it is not possible to be dogmatic about which particular measures were critical in preventing SA5385 transmission. Back and colleagues [37] also found that intensive microbiological surveillance (IMS) and mupirocin use was needed to control a MRSA outbreak in neonates, but mupirocin was ineffective at eradicating MRSA colonization. Notably, IMS alone was effective at controlling an outbreak recurrence.

Desiccation resistance studies showed that SA5385 behaved similarly to other *S. aureus* strains. However, surface type onto which bacteria were inoculated had a marked effect on viability. Stomahesive is highly absorbent, and the hydrated environment allowed the survival of *S. aureus* for at least 71 days. Initially, SA5385 showed increased resistance to desiccation compared with the other strains studied, and this may give PT 53,85 a selective advantage. As Stomahesive is frequently coated *in situ* by sweat and oro-nasal secretions, we examined the effect of serum on bacterial desiccation. Inoculated Stomahesive plus serum consistently had lower bacterial death rates than other environments, suggesting that serum aids persistence. We have not proved a causal link between endemic spread of *S. aureus* and Stomahesive use, but have shown that this material provides a survival niche for bacteria. Of 12/19 UK neonatal units replying to a postal questionnaire, 2 use Stomahesive, 3 other materials, and 3 Friar's balsam as skin protectant materials (4 are not using any measures). Clearly, materials which favour bacterial survival must be used with care in individuals with such heightened susceptibility to infection [38].

In summary, we experienced a 5-year outbreak of a MSSA strain which was detected and monitored by routine, weekly, phage typing of all *S. aureus* isolates, and subsequently confirmed by DNA fingerprinting. Successful control of the outbreak was only achieved after deficiencies in the handling of a skin protectant material were identified and a new protocol instigated. Empirical use of mupirocin was also implemented for babies known to be colonized/infected by *S. aureus*. *In vitro* data supported clinical observations that Stomahesive can provide a survival niche for *S. aureus*. New epidemic *S. aureus* strains have continued to emerge and decline for unknown reasons. Delineation of the factors which determine the ability of strains to spread epidemically will be of value in controlling the dissemination of both MSSA and MRSA clones.

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