Babies and Bacteria: Phage Typing, Bacteriologists, and the Birth of Infection Control

KATHRYN HILLIER

SUMMARY: During the 1950s, *Staphylococcus aureus* became a major source of hospital infections and death, particularly in neonates. This situation was further complicated by the fact that *Staphylococcus* quickly gained resistance to most antibiotics. Controlling these infections was a pressing concern for hospital workers, especially bacteriologists who tackled it through the use of a new epidemiologic tool: phage typing. This article argues that during the mid- to late 1950s a series of staphylococcal hospital and nursery epidemics united phage typers, brought international recognition to the usefulness of their technique, and, in the process, contributed to the establishment of the new field of infection control. Through the use of this new tool, phage typers established themselves as experts in infection control and, in some places, became essential members of newly formed infection-control committees. The nursery epidemics represent a particularly important test for phage typing and infection control, for this staphylococcal strain (80/81) was especially virulent and spread rapidly beyond the hospital to the wider community. The epidemiologic information provided by phage typers was vital for devising practical advice on how to control this deadly strain of *Staphylococcus* and also for transforming the role of the hospital bacteriologist from mere technician into infection-control expert.

KEYWORDS: phage typing, infection control, *Staphylococcus*, hospital bacteriology, nursery infection, hospital infection, antibiotics, epidemiology

"Death from the Hospital Nursery" was announced in the pages of the *Ladies' Home Journal* in February 1959, evoking fear in the minds of parents all over the United States.[1] This article, with its emotive language, represented the popular response to nearly half a decade of sudden,

This research was supported by a University of Sydney Post Graduate Award (UPA). Many thanks to the Archives of the Royal Prince Alfred Hospital in Sydney for their help with this project.

1. Gladys Denny Shultz, "Death from the Hospital Nursery," *Ladies' Home Journal*, February 1959, pp. 60–61, 178–80.

almost explosive incidences of staphylococcal infections in hospital nurseries. The alarm generated by this article and, more generally, by the frequency of troublesome staphylococcal infections in hospitals was in direct contradiction to the expectations formed just twenty years earlier at the beginning of the antibiotic era. Antibiotics were meant to signal the end of bacteriology and bacteriological diseases: no longer would bacteriologists need to be bothered with identifying or characterizing bacteria because penicillin, the magic bullet of 1941, was predicted to defeat all the bacterial diseases that had plagued mankind for centuries.[2] This "wonder drug," together with other newly released antibiotics during the 1940s and 1950s, was also expected to have curative properties against viral or even cancerous diseases. These initial promises were not fulfilled.

Bacteriologists, most specifically those who worked in hospital settings, were kept busier than ever from the onset of the antibiotic era. In the early days of antibiotic therapy, they were responsible for reconstituting the penicillin powder, readying it for injection; later, as more antibiotics became available, they were responsible for identifying the type of infecting organism so that the correct antibiotic could be prescribed.

Initial reactions to penicillin were optimistic: it was extremely active against many of the most common bacteria. However, one bacterium in particular presented an early and ongoing challenge to the promise of life without infection. Just as the conquest story of penicillin was being immortalized in print, resistance to it was noted.[3] *Staphylococcus aureus* was identified as the main culprit, and the antibiotic era was therefore closely, and ironically, followed by what is known as the "Golden Staphs" era.

2. Most readers will be familiar with the traditional story of the discovery of penicillin by Alexander Fleming in 1928, and Howard Florey's later recognition of its potential therapeutic use. For a historical account of these events, see Jonathan Liebenau, "The British Success with Penicillin," *Soc. Stud. Sci.*, 1987, *17*: 69–86; Robert Bud, "Many Happy Recoveries," *New Scientist*, June 1996, p. 48; Donna Hoel and David N. Williams, "Antibiotics: Past, Present and Future: Unearthing Nature's Magic Bullets," *Postgrad. Med.*, 1997, *101* (1): 114–22; Eric Lax, *The Mold in Dr. Florey's Coat: The Story of the Miracle of Penicillin* (New York: Holt, 2004).

3. For example, two books appeared in 1945 and 1946 that were filled with praise for penicillin, while at the same time Amedo Bondi and Catherine Dietz had begun to publish articles regarding its failure against seemingly resistant bacteria: see J. D. Ratcliff, *Yellow Magic* (Scranton, Pa.: Random House, 1945); George Bankoff, *The Conquest of Disease: The Story of Penicillin*, The Conquest Series (London: Macdonald, 1946); Amedo Bondi, Jr., and Catherine C. Dietz, "Penicillin Resistant Staphylococci," *Proc. Roy. Soc. Med.*, 1945, *55*: 55–58; Bondi and Dietz, "Production of Penicillinase by Bacteria," *Proc. Soc. Exper. Biol. & Med.*, 1944, *56*: 132–34; Bondi and Dietz, "Relationship of Penicillinase to the Action of Penicillin," ibid., pp. 135–37.

The emergence of deadly staphylococcal infections demanded a drastic reconceptualization of this bacterium that was, at one time, greeted "nonchalantly by the clinician with the remark 'Only old Staph.'"[4] In contrast, by the end of the 1950s a diagnosis of a staphylococcal infection would receive serious attention, for a graze on the skin could potentially lead to a deadly case of staphylococcal septicemia or staphylococcal pneumonia. The sudden increase in staphylococcal hospital infections marked a major challenge to hospital workers worldwide, who were slowly beginning to realize that antibiotics were powerful yet complex drugs that needed to be used carefully.

One response to staphylococcal infections in hospitals was the use of phage typing to follow the spread of individual infecting strains through an institution, thereby gaining epidemiologic knowledge that could be used in formulating plans to combat and stop the infections. Phage typing is a technique that exploits the property of phages (also known as bacterial viruses, or bacteriophages) to infect bacteria selectively. "Phage" is derived from the Greek *phagein* (to eat); thus phages are viruses that "eat" (infect) bacteria. Each strain of bacterium is susceptible to infection by only a small number of phages; by discovering these different susceptibilities, a unique "phage-typing pattern" is determined for each strain. Bacterial strains can thus be differentially identified through their reactions to specific phages: in the presence of phages, susceptible bacteria will burst or lyse, which leads to the formation of a clear spot on an otherwise opaque bacterial culture. Bacteriologists had, for a long time, been troubled by their inability to definitively identify a common infectious source during outbreaks of epidemic or nosocomial infections. In the early twentieth century, serological typing was used to differentiate strains of *Streptococcus*, and was later developed (with equivocal results) for use with *Staphylococcus*, as discussed below. Phage typing, however, had the potential to be a more specific technique and was developed to identify

4. This comment was made in a report found in the papers of Dr. E. D. G. Murray, MG30, B91, 24-21.14, National Archives of Canada, Ottawa (hereafter Murray Papers). Other authors have written about the unique relationship between staphylococci and antibiotics: see Donald J. McGraw, "The Golden Staph: Medicine's Response to the Challenge of the Resistant Staphylococci in the Mid-Twentieth Century," *Acta Hispanica ad Medicinae Scientiarumque Historiam Illustrandam*, 1984, *4*: 217–19; Craig H. Steffee, "Penicillins and Staphylococci: A Historical Interaction," *Perspect. Biol. & Med.*, 1992, *35*: 596–608; Melinda D. Maranan, Beatrix Moreira, Susan Boyle-Vavra, and Robert S. Daum, "Antimicrobial Resistance in Staphylococci," *Infect. Dis. Clin. North America*, 1997, *11*: 813–49. McGraw and Steffee, especially, contextualize the relationship between penicillin and *Staphylococcus*.

strains of staphylococci in the mid-1940s;[5] nevertheless, it remained relatively unknown until the time of the first serious outbreaks of nursery infection in the mid-1950s.

Phage typing became another responsibility assumed by hospital bacteriologists in the early days of the antibiotic era. Because staphylococci are ubiquitous and can be found on the skin, nasal hairs, or even perinea of healthy people, it was important to ascertain whether patients were becoming infected with their own strains, or with those carried by hospital staff, or found on the hospital equipment, or brought in by visitors, or even circulating freely in the hospital air. Knowing the origin of the infecting strains would assist with strategies to stop cross-infections.

A particularly virulent strain of *Staphylococcus*, named "80/81," was discovered in Australia in 1954 and very soon after in Canada, and was soon pandemic throughout hospitals and communities worldwide. This pandemic was worrisome because it occurred in the very early days of the antibiotic era. The outbreaks of nursery infections represented one of the first times that phage typers had been brought together in the battle against *Staphylococcus*. The epidemics not only brought worldwide attention to the problem of hospital cross-infection, but also brought recognition to phage typing as a useful tool for understanding the epidemiology of antibiotic-resistant staphylococcal infections. Phage typers took advantage of their time in the spotlight not only to "unravel the chains of infection" but also to provide practical solutions designed to halt the spread of infection.[6] Locally, phage typers and bacteriologists used their epidemiologic findings to assert their expertise in the hospi-

5. Graham S. Wilson and D. Atkinson, "Typing of Staphylococci by the Bacteriophage Method," *Lancet*, 1945, *1*: 647–49. It was Wilson and Atkinson's methods and strains that were adapted for use by phage typers during this period; however, their work was based on earlier attempts by others to create a typing system for *Staphylococcus*. See Roy T. Fisk, "Studies on Staphylococci I: Occurrence of Bacteriophage Carriers among Strains of *Staphylococcus aureus*," *J. Infect. Dis.*, 1943, *71*: 153–60; Fisk, "Studies on Staphylococci II: Identification of *Staphylococcus aureus* Strains by Means of Bacteriophage," ibid., pp. 161–65; Frank Macfarlane Burnet and Margot McKie, "Type Differences amongst Staphylococcal Bacteriophages," *Austral. J. Exper. Biol. & Med. Sci.*, 1929, *6*: 21–31; Stanley Williams and Cecily Timmins, "An Investigation of the Source of Staphylococcal Infection in Acute Osteomyelitis," *Med. J. Australia*, October 1938, pp. 687–98.

6. This phrase is taken from a 1981 interview with Phyllis Rountree, one of the chief investigators of the nursery epidemic: Kerry Gordon and Victoria E. Barker, *Phyllis Margaret Rountree: Honorary Research Associate in the School of Microbiology, the University of New South Wales, University Interviews Project* (Sydney: University of New South Wales, 1991), p. 22. Rountree identified this episode in her career as the most important work she ever did. She was well placed to take on phage typing, as she had been educated by Wilson.

tal, to suggest administrative changes in the management of postnatal care, and to assure themselves roles on newly created infection-control committees.[7] Incidences of infection caused by 80/81 fell drastically in the early 1960s; however, by this time hospital bacteriologists had already cemented their roles as infection-control experts, a role they continue to fulfill to this day.

Before the nursery epidemics, most hospital administrators and clinicians regarded bacteriologists simply as technicians, whose work was restricted to the laboratory where they performed mundane tests and had no authority to participate in the management of patient care. From the 1950s onward, however, as bacteriologists became increasingly recognized as infection-control specialists, they began to assert their opinions and expertise beyond the laboratory and into the wards and meeting rooms of the hospital. Much of this transformation in the role of bacteriologists can be attributed to the unique data and insight that they could contribute to the problems surrounding staphylococcal infections in the early (and confusing) days of the Golden Staphs era. Traditional accounts of the history of infection control tend to omit the important role played by phage typers in providing both the essential scientific data needed for understanding how these infections spread and methods for controlling cross-infection. This gap may be attributed to the fact that the knowledge obtained and provided by bacteriologists was quickly assimilated into the common knowledge of all concerned: physicians, surgeons, nurses, administrators, and general hospital staff. In this article I aim to address this gap by providing an additional perspective on the history of hospital infection control during its early days in the 1950s and 1960s.

The Appearance of Strain 80/81

In May 1952, during an intensive study of nursery infections at the Royal North Shore (RNS) Hospital in Sydney, five babies were observed to have staphylococcal lesions "somewhat different in character from those usually seen."[8] These included breast abscesses in mothers infected from

7. The predominance of bacteriologists' presence on infection-control committees requires more study. As I argue here, their inclusion in these committees represented the ideal situation, as many of the infection-control manuals of the time stipulated. However, this ideal could not be achieved everywhere: see the articles on "Surveillance" in Robert E. O. Williams and R. A. Shooter, eds., *Infection in Hospitals: Epidemiology and Control* (Oxford: Blackwell Scientific Publications, 1963), pp. 323–49.

8. Clair Isbister, Beatrix E. Durie, Phyllis M. Rountree, and Barbara M Freeman, "A Further Study of Staphylococcal Infection of the New-Born," *Med. J. Australia*, December

skin lesions in babies that did not respond well to penicillin therapy. This observation caused the chief researchers, Dr. Clair Isbister (a pediatrician) and Dr. Beatrix Durie (a pathologist), to call on Dr. Phyllis Rountree, a bacteriologist from the Royal Prince Alfred (RPA) Hospital across town. They hoped that Rountree could use the relatively new technique of phage typing to determine which strains were infecting the babies.[9] Rountree had recently organized a staphylococcal reference laboratory at the RPA, funded by the National Health and Medical Research Council (NH&MRC) of Australia, which was responsible for typing staphylococci from hospitals throughout Australia and New Zealand.

Isbister, who had been investigating nursery infections for some time, had a suspicion that the lesions found at the RNS were caused by an epidemic strain of *Staphylococcus*, so Rountree decided to track the strain's dissemination through its victims, carriers, and the hospital environment using phage typing.[10] The strain initially could be typed only by using modified phages—that is, ones that were chemically altered from those found in the standard set of typing phages—and this indicated that this strain

---

1954, pp. 897–900, on p. 897. This was a clinical observation of the wounds, and not a bacteriological finding. Indeed, Isbister and Rountree later disagreed over the possibility of making such observations without bacteriological evidence: personal communication, Dr. Clair Isbister, 31 October 2001. M. T. Parker has also described the events surrounding the 80/81 outbreak, although in an abridged version: M. T. Parker, "The Significance of Phage-Typing Patterns in *Staphylococcus aureus*," in *Staphylococci and Staphylococcal Infections*, vol. 1, *Clinical and Epidemiological Aspects*, ed. C. S. F. Easmon and C. Adlam (Sydney: Academic Press, 1983), pp. 33–62.

9. Personal communication, Clair Isbister, 31 October 2001. Rountree had long had an interest in phage that began when she was a researcher working alongside Macfarlane Burnet in the mid-1930s.

10. Both Rountree and Isbister received outside funding for their research: Rountree's phage-typing reference laboratory at the Royal Prince Alfred Hospital was funded by the Australian National Health and Medical Research Council; Isbister's work was done under a grant from the King George V and Queen Mary Maternal and Infant Welfare Foundation. The two researchers had different motives and aims for their research: Isbister was working from a clinical point of view, while Rountree approached the problems as a scientist. These differences came to a head in the course of their research when Isbister insisted that she could differentiate strains clinically, but Rountree was adamant that this could only be done using phage typing: personal communication, Clair Isbister, 31 October 2001. It is also important to note at this point that in Australia there was no organized research institution concerned with the diseases of children. When an institute was organized in the late 1950s by Dr. Lorimer Dods, its primary focus was on severe chronic diseases such as leukemia, glandular conditions, and muscular dystrophy: see "Child Health Research Body Formed," *Sydney Morning Herald*, 20 June 1958, p. 5; "Five Little Mites in Tragedy Ward," *Sun Herald*, 10 August 1958, p. 41.

was something new. One month later, this same strain of *Staphylococcus* was responsible for an outbreak in a country hospital in Victoria. At this point, Rountree initiated a study of the incidence of all staphylococcal infections at the RNS, which continued until the end of September 1953. She found that nearly half the strains found in the hospital belonged to the original pattern, but that it disappeared in April 1953, only to be replaced in June by yet another untypable strain. This second strain caused the same sort of pustular skin lesions as the previous strain and was also labeled an "epidemic" strain by Isbister and Rountree in January 1954. Again, the new strain could be typed only with modified phages.

During these investigations, Rountree was in constant consultation with Dr. Robert E. O. Williams of the Staphylococcal Reference Laboratory at Colindale in London, England, regarding the new strain and the development of her new, modified phage. Rountree and Williams were two of twelve founding members of the International Subcommittee for Phage Typing of Staphylococci, organized in September 1953 at the International Microbiology Congress in Rome.[11] Colindale acted as the point of reference for phage typers across the world: from here they received their phages and their standardized methods.[12] Rountree first wrote to Williams in March 1954, asking him to check the RNS strain and the new phage against those held in his laboratory, including the phage used to type a strain responsible for a mastitis epidemic in Canada.[13] Williams wrote back in May 1954 to confirm that Rountree's strain could not be typed by any of the phages in the basic set of typing phages, nor by the phages used in the Canadian epidemic. It was therefore clear that the strain was new and unique, and in October 1954 Williams assigned the

11. The Subcommittee's original members represented twelve nations: the United Kingdom (Williams), France (R. Wahl), Northern Ireland (V. D. Allison), the United States (J. E. Blair), Italy (G. Buonomini), Denmark (K. Eriksen), the Netherlands (R. Kooy), Poland (R. Pakula), Norway (T. Vogelsang), Sweden (G. Wallmark), Canada (E. Bynoe), and Australia (Rountree). Each member was meant to act as a liaison between phage typers in his or her country and Williams at Colindale, where the standardized phages were kept.

12. Robert E. O. Williams and Joan E. Rippon, "Bacteriophage Typing of *Staphylococcus aureus*," *J. Hygiene*, 1952, *50*: 320–53. For more contextualization of how this committee operated, see Bettina B. Wentworth, "Bacteriophage Typing of the Staphylococci," *Bacter. Rev.*, 1963, *27*: 253–72.

13. Phyllis Rountree to R. E. O. Williams, 16 March 1954, Papers of P. M. Rountree, MLMSS 6482, box 2, State Library of New South Wales, Sydney (hereafter Rountree Papers). The mastitis epidemic discussed here is probably the one described by Webb in 1954 regarding a study conducted in 1947–51: Jean F. Webb, "Newborn Infections and Breast Abscesses of Staphylococcal Origin," *Can. Med. Assoc. J.*, 1954, *70*: 382–88.

new phage the designation "80" in the basic set of typing phages held at Colindale.[14]

Isbister and Rountree submitted a paper describing their research to the *Medical Journal of Australia* for publication in December 1954.[15] In July 1955 Rountree further detailed the appearance and prevalence of the strain, using the designation "80" for the first time in print; she explained that it had appeared in the general hospital population around February 1954, but that a concurrent survey of blood donors had revealed no carriers of strain 80, indicating that it had not spread to the wider community.[16] Strain 80 was still a hospital strain, similar to most other infective strains of *Staphylococcus*: they caused problems in the hospital but did not migrate to the community outside.

At this point, strain 80 was unique to Australia; Williams wrote to Rountree in October 1954 that "it is, therefore, rather like your earlier phage 31B, which while undoubtedly useful to you did not seem to be a great deal of use to us here."[17] He saw no reason to consider the new phage for inclusion in the standard set of phages. Rountree, remembering Williams's comments years later, remarked: "Perhaps, they said, it was only a local thing and wasn't very important."[18]

Meanwhile in Canada, workers at the Laboratory of Hygiene, Department of National Health and Welfare, had also encountered a new infective strain of *Staphylococcus* during their survey of hospital infections at an Ottawa hospital conducted from March 1953 to March 1954 (i.e., in the months immediately after Rountree's investigations at the RNS Hospital). The investigators, Dr. Evan T. Bynoe, Dr. R. H. Elder, and Dr. R. D. Comtois, discovered a novel infective strain that could be typed only with a new phage developed by them, which came to be known as "81." This strain was the causative agent in half the observed cases of boils and abscesses in the Ottawa hospital. Bynoe's 1956 paper on the study reported a situ-

14. It has long been a contentious issue for phage typers that the assignment of numbers for phages is more or less haphazard, in that it is based on the order of their discovery, which in no way indicates the biochemical relationships between different phages.

15. Isbister et al., "Further Study of Staphylococcal Infection" (n. 8). This article makes no mention of the fact that the new phage was named "80," but this is probably because the designation had only been assigned in October.

16. Phyllis M. Rountree and Barbara M. Freeman, "Infections Caused by a Particular Phage Type of *Staphylococcus aureus*," *Med. J. Australia*, July 1955, pp. 157–61. Rountree used members of the public who donated blood at the RPA for this study.

17. Williams to Rountree, 19 October 1954, Rountree Papers, MLMSS 6482, box 2.

18. Gordon and Barker, *Phyllis Margaret Rountree* (n. 6), p. 19.

ation similar to Rountree's.[19] Although the phages themselves were later found to have different biochemical properties, Rountree's and Bynoe's bacterial strains were identical.[20] Because the typing pattern of this strain reflected both of the typing phages, it became known as "80/81."

Strain 80/81, first identified in Sydney and Ottawa, quickly spread over the globe, creating a sudden need for competent phage typers. In the process, it also contributed to the loss in popularity of an alternative technique for the differentiation of staphylococci: serological typing, developed by Per Øeding, a Norwegian bacteriologist, in 1952. Serological typing was eclipsed for two reasons: at the time of the nursery epidemics, there was no international network for serological typing, nor was there a Colindale-type laboratory willing to organize bacteriologists worldwide who wished to use the technique. Phage typing, on the other hand, was both accessible and standardized. Williams and Øeding later collaborated on a paper comparing the two methods and concluded that phage typing was preferable for its superior epidemiologic usefulness in recognizing more types than the serological method, and enabling investigators to make distinctions between types based on a greater number of different reactions.[21] The article also stated that "phage typing has been widely employed in epidemiological studies" and that "serological typing has hitherto been far less widely used for comparable epidemiological studies, but it too has proved satisfactory in the hands of certain investigators."[22] Serological typing was thus characterized as useful for research on a smaller scale and as a specialist tool in unique situations. With phage

19. Evan T. Bynoe, R. H. Elder, and R. D. Comtois, "Phage-Typing and Antibiotic Resistance of Staphylococci Isolated in a General Hospital," *Can. J. Microbiol.*, 1956, *2*: 346–58.

20. This finding was conceptually difficult for the researchers to accept, because until that time strains had always been typed by phages with the same biochemical characteristics. Staphylococcal phages belong to about eight to ten different serological groups, as determined by their reactivity to antibacteriophage sera prepared in rabbits; four of these groups, designated I, II, III, and IV, contain the majority of the typing phages. Strains of staphylococci typically react with phages from only one group; therefore, a single strain will be typed by phages within just one of the four groups of typing phages. In this case, however, strains 80 and 81 were actually identical but could be typed by both phage 80, which serologically belonged to group I, and phage 81, which displayed serological characteristics common to groups I and III—a previously undescribed situation, and thus a very confusing one for prominent phage typers such as Rountree, Bynoe, and Williams who were working to promote the technique.

21. Per Øeding and Robert E. O. Williams, "The Type Classification of *Staphylococcus aureus*: A Comparison of Phage-Typing with Serological Typing," *J. Hygiene*, 1958, *56*: 445–54, on p. 453.

22. Ibid., p. 445.

typing established as the hegemonic preference for typing staphylococci, phage typers were kept busy for the next ten years identifying sources and pathways of infection as well as serving on infection-control committees and advising on pharmacological and managerial solutions for infection. This increase in phage-typing activity can be measured by the proliferation of phage-typing articles published during the late 1950s and early 1960s.[23]

The Worldwide 80/81 Pandemic

The de novo, nearly simultaneous appearance of the same strain of *Staphylococcus* in two countries separated by an ocean presented a scientific curiosity for Rountree, Bynoe, and Williams. But when the virulence and frequent incidence of the strain became apparent, curiosity quickly turned to concern. As reported by Rountree in 1955, strain 80/81 was responsible for nineteen out of twenty-three outbreaks of neonatal staphylococcal infections occurring in Australian hospitals. She also observed that its prevalence as an infecting agent in general hospital wounds was increasing, and that not all babies who carried *Staphylococcus* in the hospital showed signs of infection, but instead were simply carriers of the strain.[24] However, once these babies returned home, the strain spread easily to family members who did suffer infection; this was the first time a so-called hospital strain of *Staphylococcus* was observed to spread rampantly to the wider community.[25] When adults and older children sought treatment,

23. This claim is based on a survey of *Index Medicus* for the years 1945–56. In the years 1945–54, the number of articles dealing with staphylococcal infection averaged 49 per year. In contrast, for the two years 1955–56, marking the beginning of the Subcommittee period, the average jumped to 92.5, and many of these articles featured phage typing as a method of study.

24. Rountree and Freeman, "Infections Caused by a Particular Phage Type" (n. 16).

25. This initial observation by Rountree is repeatedly supported by the work of later investigators. See, e.g., Jack N. Baldwin, Mevin S. Rheins, Robert F. Sylvester, and Thomas E. Shaffer, "Staphylococcal Infections in Newborn Infants: III, Colonization of Newborn Infants by *Staphylococcus pyogenes*," *Amer. Med. Assoc. J. Dis. Child.*, 1957, *94*: 107–16; John E. Blair and Miriam Carr, "Staphylococci in Hospital-Acquired Infections," *JAMA*, 1958, *166*: 1192–96; E. S. Duthie, "Generalized Staphylococcal Epidemics in a Hospital Group," in *Symposium on Hospital Coccal Infections* (n.p., 1957), pp. 23–25; editorial, "Trouble in the Nursery," *Can. Med. Assoc. J.*, 1960, *83*: 1112–13; F. Robert Fekety, Leon Buchbinder, Elmer L. Shaffer, Sidney Goldbery, Preston Price, and Louis A. Pyle, "Control of an Outbreak of Staphylococcal Infections among Mothers and Infants in a Suburban Hospital," *Amer. J. Pub. Health*, 1958, *48*: 298–309; Valerie Hurst and Moses Grossman, "The Hospital Nursery as a Source of Staphylococcal Disease among Families of Newborn Infants," *New England J. Med.*, 1960, *262* (19): 951–56; Althea D. Kessler and Roland B. Scott, "Staphylococcal Infections in

the strain was then reintroduced into the hospital. During the mid- to late 1950s, 80/81 became a major cause of wound infection and staphylococcal septicemia. Rountree concluded that "evidence is presented for regarding this staphylococcus [*sic*] as one of enhanced virulence."[26]

By the mid-1950s, 80/81 was wreaking havoc in Australia and New Zealand and was troublesome in Canada and Great Britain, but its true prevalence became apparent only in June 1956 when a letter appeared in the *Journal of the American Medical Association* from Dr. Thomas E. Shaffer of the Department of Bacteriology at Ohio State University, asking for cultures of pustular lesions from any physician experiencing a staphylococcal outbreak.[27] Shaffer described epidemics of micrococcal (staphylococcal) infection occurring in seven hospitals across the northern and eastern United States that typed as 42B/47C/44A/52 (i.e., it was sensitive to phages 42B, 47C, 44A, and 52).[28] Rountree's interest was immediately

---

Young Infants," *Amer. Med. Assoc. J. Dis. Child.*, 1958, *96*: 294–98; Walter A. Murray, Gerald E. McDaniel, and May Reed, "Evaluation of the Phone Survey in an Outbreak of Staphylococcal Infections in a Hospital Nursery for the Newborn," *Amer. J. Pub. Health*, 1958, *48*: 310–18; Phyllis Rountree and Mary Beard, "Further Observations on Infection with Phage Type 80 Staphylococci in Australia," *Med. J. Australia*, December 1958, pp. 789–95; Thomas E. Shaffer, Robert F. Sylvester, Jack N. Baldwin, and Mevin S. Rheins, "Infections in Newborn Infants: II. Report of 19 Epidemics Caused by an Identical Strain of *Staphylococcus pyogenes*," *Amer. J. Pub. Health*, 1957, *47*: 990–94; Richard T. Smith, "The Role of a Chronic Carrier in an Epidemic of Staphylococcal Disease in a Newborn Nursery," *Amer. Med. Assoc. J. Dis. Child.*, 1958, *95*: 461–68; Morag C. Timbury, T. S. Wilson, J. G. P. Hutchison, and A. D. T. Govan, "A *Staphylococcus* Type-80 Epidemic in a Maternity Hospital: Illustrating Some Special Features," *Lancet*, 1958, *2*: 1081–84. Strains of *Streptococcus*, of course, were known to often spread from the hospital to the community and back; see Irvine Loudon, *The Tragedy of Childbed Fever* (New York: Oxford University Press, 2000).

26. Rountree and Freeman, "Infections Caused by a Particular Phage Type" (n. 16), p. 161.

27. Thomas E. Shaffer, "Epidemics of Micrococcic Infections in Infants," *JAMA*, 1956, *161* (5): 475. The full extent of its spread is not known, because only a few countries with access to phage typing could devote time and money to these sorts of epidemiologic studies—although the organism was found in 1958 to be prevalent in Uganda, for example, by an expatriate working there: R. S. F. Hennessey and R. A. Miles, "*Staphylococcus aureus* Type 80 and Human Infections in Uganda," *Brit. Med. J.*, 1958, *2*: 893–95.

28. Shaffer did not mention the dilution of phage that he used in his typing, which is a necessary piece of information for standardized reporting of phage-typing results. See Williams and Rippon, "Bacteriophage Typing" (n. 12). Shaffer's nonadherence to the standard procedure as established by Williams and recognized by the Subcommittee is perhaps best explained by the fact that this was still a relatively new procedure in the United States at the time. See Blair and Carr, "Staphylococci in Hospital-Acquired Infections" (n. 25); Matthew H. Fusillo, Richard N. Roerig, and Kenneth F. Ernst, "Phage-Typing the Antibiotic-Resistant Staphylococci: IV. Incidence and Phage Type Relationship of Antibiotic-Resistant Staphylococci among Hospital and Nonhospital Groups," *Antib. & Chemother.*, 1954, *4*: 1202–9.

sparked by this appeal, and she wrote to Shaffer in August 1956 to tell him about similar outbreaks on her side of the world. She requested his strains, for she suspected they were identical to hers. To this Shaffer responded immediately:

> We have been familiar with your interest in this field. . . . Some representative subcultures of organisms obtained from separate epidemics in this country will be sent to you at once. . . . We have used phage 81 and find it reacts with our organisms specifically. . . . We have wondered whether this phage is not identical with your 80.[29]

The two scientists exchanged strains and phages, and, as expected, the organism responsible for the epidemics in the United States was the same one that had been encountered originally by Rountree in 1953 and by Bynoe in 1953–54. Subsequent articles concerning Shaffer's epidemic carried the footnote that further investigation had revealed that the American strain, first identified as 42B/47C/44A/52, now typed as 80/81.[30] Rountree remembered that by 1958 "it [strain 80/81] was reported by every country which had the typing system and was interested in these staphylococci."[31]

Strain 80/81 was the most devastating strain of *Staphylococcus* that had been encountered by clinicians and phage typers. During the nursery epidemics of the 1950s, investigators witnessed a "sudden, almost explosive, appearance of infections in an institution."[32] The infections caused by the nursery epidemic strain were particularly severe, producing "pustular skin lesions with surrounding cellulitis in babies, breast abscesses in mothers and babies, and severe boils in nurses."[33] The worst epidemic in the early years occurred in November 1955 at a large private hospital in Christchurch, New Zealand, where an outbreak of staphylococcal skin

29. Shaffer to Rountree, 10 August 1956, Rountree Papers, MLMSS 6482, box 2. It is interesting to note that, although Shaffer had obtained phage 81 from Bynoe, he did not know about its relationship to phage 80, information that Bynoe could have provided.

30. Baldwin et al., "Staphylococcal Infections" (n. 25). Subsequent investigations into the nature of phages 42B, 44A, and 52 revealed that they had undergone some variation and were no longer diagnostically identical to their parent, standard phages held at Colindale; these phages were therefore collected from typing laboratories in the United States and new phages from Colindale were distributed. See John E. Blair and E. T. Bynoe, "Variation in Three Staphylococcal Typing Phages," *U.S. Pub. Health Rep.*, 1958, *73*: 465–66.

31. Gordon and Barker, *Phyllis Margaret Rountree* (n. 6), p. 19. In 1958, there were twenty-two countries represented on the International Subcommittee for Phage Typing of Staphylococci.

32. Blair and Carr, "Staphylococci in Hospital-Acquired Infections" (n. 25), p. 1194.

33. Parker, "Significance of Phage-Typing Patterns" (n. 8), pp. 49–50.

lesions culminated in numerous cases of pneumonia, causing the death of eight infants aged between fifteen and twenty-three days and forcing closure of the maternity wing of the hospital.[34]

Incidences of staphylococcal infection in nurseries and on the general wards of hospitals eventually caught the attention of the public media, with the number of newspaper articles regarding antibiotic-resistant staphylococci increasing throughout the 1950s. The first articles of the early 1950s simply stated that bacteria resistant to penicillin were appearing in hospitals. Over time, newspapers began to focus on the needless overuse of drugs and advocated prescribing drugs with more care—although these concerns were often inspired by economic factors, especially in Australia, where penicillin was provided free of charge via the federal government's newly enacted Pharmaceutical Benefits Act.[35] The first feature article regarding antibiotics and resistant staphylococci appeared in the *Sydney Morning Herald* in July 1952. This article served to warn the public about the problems of the indiscriminate use and overprescription of antibiotics, but also provided reassurances that research into this problem was continuing. It compared the development of antibiotics to that of the automobile: "The early failure of all kinds of horseless carriages didn't stop the evolution of the motor car of today."[36] This was not an age of pessimism.

Strain 80 made its first appearance in the popular press in December 1955, but Sydneysiders, as far as can be ascertained by media coverage, were not overly worried about strain 80 in relation to nursery infections, probably because few deaths had occurred.[37] During the winter of 1957, however, when strain 80 complicated cases of influenza and caused the deaths of several people, calls were made for public inquiries and governmental studies, and for serious staphylococcal infection to be made a notifiable illness.[38] Staphylococcal illnesses were also the subject of magazine

34. D. W. Beaven and A. F. Burry, "Staphylococcal Pneumonia in the Newborn: An Epidemic with 8 Fatal Cases," *Lancet*, 1956, *2*: 211–15.

35. "Germs 'Resisting' New Drugs," *Sydney Morning Herald*, 1 June 1950, p. 1; "Inquiry Is Planned: Needless Use of Drugs," ibid., 5 June 1950, p. 14; "Some Doctors Are Using Four Rare Drugs Unnecessarily," ibid., 24 October 1950, p. 20; "Move to Check Run on Scarce Drugs," ibid., 2 December 1950, p. 4.

36. "'Wonder' Drugs are at the Crossroads. . . . Some Users Make Them Blunder Drugs," *Sunday Herald*, 20 July 1952, p. 9.

37. "Warnings to Doctors on Drug Misuse," *Sydney Morning Herald*, 15 December 1955, p. 4.

38. "Warning on 'Virulent Infection,'" *Sydney Morning Herald*, 16 August 1957, p. 1; "Government to Set Up Flu Advisory Committee," ibid., 17 August 1957, p. 1; "Govt. Seeks Reports of Gold[en] Staph[lyococcus]," ibid., 21 August 1957, p. 1; "Concern at

and newspaper articles in the United States during this period. The *New York Times* first reported on strain 81 in October 1957, and subsequent articles repeatedly described antibiotic misuse and problematic hygienic routines as well as calling for governmental intervention in the epidemics.[39] In addition to the reports in major newspapers, magazines such as the *Ladies' Home Journal* also picked up stories on *Staphylococcus*.[40]

In all popular articles dealing with *Staphylococcus* and antibiotics, the work of phage-typers—bacteriologists—was featured, and they were represented as experts. This is reflective of the new role of hospital bacteriologists in the field of infection control. They came to occupy positions in all types of hospital departments and became experts on not only nursery infections but also wound infections, septicemia, and bone infections. They were ideally placed in hospitals to acquire a shared and central body of data regarding a hospital-wide problem: they could act as liaison points for contact between workers from different parts of the hospital experiencing similar outbreaks of staphylococcal infection.

Within the hospital, one of the ways bacteriologists found their voice during the 80/81 epidemics was by suggesting changes in postnatal care. On the surface, a bacterial nursery epidemic is a problem that seems to be purely technical, and the initial use of a technical tool to address it, phage typing, reflects this conceptualization. Identification of the strains, antibiotic treatment of the sick, and stricter aseptic and antiseptic practices should have been enough to halt this epidemic—but the answer was not as simple as this. Lacking a pharmacological solution, phage typers drew on the growing body of their research findings to pinpoint problems in the management of postnatal care. By the 1960s, more than a decade of epidemiologic studies into nursery infection had convinced researchers that the nursery was the nidus of infection. They also agreed that infection passed from older neonates to incoming newborns, a mode

---

Gold[en] Staph[ylococcus] Resistance," 21 August 1957, p. 4; "Two More Sydney Golden Staph[ylococcus] Deaths Reported," ibid., 22 August 1957, p. 3; "Serious Staph[ylococcus] Infection to Be Notifiable," ibid., 27 June 1958, p. 4; "Bid to Make Staph[ylococcus Infections] Notifiable," ibid., 28 August 1958, p. 13.

39. Robert K. Plumb, "Hospitals Found in Germ Danger," *New York Times*, 17 October 1957, p. 35; "New Germ Strain Takes Heavy Toll: U.S. Studies Virulent Form of *Staphylococcus* That Resists Antibiotics," ibid., 22 March 1958, p. 19; "26 Babies Infected at 3 City Hospitals," ibid., 25 March 1958, p. 67; "Medical Parley Asked: Surgeon General Appeal in *Staphylococcus* Cases," ibid., 24 April 1958, p. 19; Robert K. Plumb, "War on Bacteria Urged by Surgeon," ibid., 16 October 1958, p. 39; Plumb, "Antibiotics Held Useless on Staph: Panelists at AMA Warn Hospitals Not to Rely on Such Agents in Infection," ibid., 12 June 1959, p. 17.

40. See n. 1. In contrast to Australia, in the United States strain 80/81 captured popular attention due to its role in nursery infection rather than in staphylococcal pneumonia.

of transmission that was accentuated by overcrowding in nurseries and by long postnatal hospital stays.[41] Overcrowding was the result of both the increased use of the hospital rather than the home for giving birth and a "baby boom" in Western countries: many hospitals simply were not built to handle the number of babies now born there, so cots in nurseries had to be situated closer together than was optimal.[42] The length of time that mothers and babies spent in the hospital after birth also was found to be directly proportional to infection rates.

Baby-to-baby transmission, however, was not the only mode by which staphylococcal infection could spread (see Fig. 1). Initially, investigators focused on nursing techniques and possible environmental vectors—especially the air, bedding, clothing, and furniture in the nursery. None of these proved to be a major infecting source, and attention soon shifted

41. Examples of papers that briefly or secondarily report problems relating to cross-infection between infants, overcrowding in nurseries, and lengthy hospital stays include J. C. Colbeck, "An Extensive Outbreak of Staphylococcal Infections in Maternity Units: The Use of Bacteriophage Typing in Investigation and Control," *Can. Med. Assoc. J.*, 1949, *61*: 557–68; Kate Campbell, "Cross Infection in the Neo-Natal Nursery," *Med. J. Australia*, August 1954, pp. 329–31; Beaven and Burry, "Staphylococcal Pneumonia in the Newborn" (n. 34); A. J. R. Clarke, A. H. McGeoch, and G. R. Sippe, "Neonatal Infection of the Skin by *Staphylococcus pyogenes*," *Med. J. Australia*, April 1956, pp. 655–58; A. Douglas and H. T. Knights, "Some Public Health Aspects of an Outbreak of Penicillin-Resistant Staphylococcal Infection in a Maternity Hospital," *New Zealand Med. J.*, 1956, *55*: 378–87; A. G. Mathew, "Experience with *Staphylococcus* Infections in a Maternity Hospital," *Med. J. Australia*, November 1956, pp. 781–86; Donald N. Wysham, Marie E. Mulhearn, Major George C. Navarre, Gerald D. LaVeck, Alfred L. Kennan, and W. R. Giedt, "Staphylococcal Infections in an Obstetric Unit. I. Epidemiologic Studies of Pyoderma Neonatorum," *New England J. Med.*, 1957, *257* (7): 295–303; Baldwin et al., "Staphylococcal Infections" (n. 25); Timbury et al., "*Staphylococcus* Type-80 Epidemic" (n. 25); W. A. Gillespie, K. Simpson, and Rosemary C. Tozer, "Staphylococcal Infection in a Maternity Hospital: Epidemiology and Control," *Lancet*, 1958, *2*: 1075–80. By the late 1950s more emphasis was placed on the above issues; articles focusing on them include Fekety et al., "Control of an Outbreak of Staphylococcal Infections" (n. 25); and Murray, McDaniel, and Reed, "Evaluation of the Phone Survey" (n. 25).

42. A trend to increased in-hospital births began in Australia, Canada, New Zealand, the United States, South Africa, and Britain in the 1920s and 1930s. The reduction in the number of home births in these countries over the first eighty years of the century was nearly 100 percent. In Britain, for example, where home births had been the norm at the beginning of the century, only 1 percent of births took place there by the early 1980s. The exodus from the home can be viewed as the general acceptance of the medicalization of birth. See Karen L. Michaelson, *Childbirth in America* (South Hadley, Mass.: Bergin & Garvey, 1988); Marjorie Tew, *Safer Childbirth?* (Melbourne: Chapman and Hall, 1990); Jessica Mitford, *The American Way of Birth* (Ringwood: Penguin Books, 1992); Judith Walzer Leavitt, "'Science' Enters the Birthing Room: Obstetrics in America Since the Eighteenth Century," *J. Amer. Hist.*, 1983, *70* (2): 281–304; Barbara Katz Rothman, *In Labor: Women and Power in the Birthplace*, 2nd ed. (London: Norton, 1991).

Figure 1. Newborns being "wheeled around" to visit their mothers, King George V Hospital, Sydney, Australia, ca. 1940s. Courtesy of Royal Prince Alfred Hospital Museum and Archives, Sydney, Australia.

to the role of the common or chronic carrier. The chronic carrier was in many cases a nurse who had a recurrent staphylococcal infection such as a boil.[43] Phage typing enabled researchers to identify these carriers, but the pathway of infection from them through the nursery took some time to establish. Nevertheless, making the conceptual shift from searching for an environmental vector of disease, such as curtains or bed linen, to a human vector, such as older neonates or the chronic carrier, was an important change of focus for bacteriological epidemiologists. Phage typing brought a new understanding of the spread of staphylococcal dis-

43. For example, Rountree identified a chronic carrier as being responsible for an outbreak of staphylococcal infection at a hospital in Maitland, New South Wales, in 1954; treatment of the offending nurse with an antibiotic nasal spray ended the outbreak: Gordon and Barker, *Phyllis Margaret Rountree* (n. 6), p. 20; George Sippe, Maitland Hospital, to Rountree, 27 April 1955, Rountree Papers, MLMSS 6482, box 2; Mathew, "Experience with *Staphylococcus* Infections" (n. 41). In some cases, however, nurses had to be excluded from duty until they were deemed to be no longer infectious.

ease, and a subsequent focus on methods of control and treatment. Of course, general hospital hygiene still was important, and its practice was strongly advocated, but bacteriologists also never missed an opportunity to comment on the indiscriminate use of antibiotics.[44]

Researchers proposed several managerial measures to contain the nursery epidemics during this period. First, babies born during the same few days should be housed together so as to prevent cross-infection between older and younger neonates. Second, infected babies should be isolated as soon as possible. Third, mothers and babies should be discharged from the hospital earlier in the postnatal period, so as to limit their exposure to infectious bacteria. Finally, short of moving birth back into the home, bacteriologists concluded that the best way to keep babies infection-free was to have them nursed at their mothers' bedsides—a practice known as "rooming-in"—for two reasons: first, mothers do not come into the hospital carrying antibiotic-resistant strains, also known as "hospital strains"; and second, babies who are roomed-in tend to be handled by fewer people and therefore are exposed to fewer infection-causing strains.[45] Because gastrointestinal infectious illnesses had been shown to be transmitted from mothers to their infants, investigators initially assumed that the same would hold for staphylococcal infections;[46] however, phage-typing investigations quickly proved this not to be the case.[47]

Rooming-in was advocated in many articles and reports regarding staphylococcal infection at this time. For example, a 1959 report published by the Ministry of Health of Great Britain noted that, "although there is not complete agreement among obstetricians concerning the

44. In the public arena, bacteriologists took every opportunity to complain about the misuse and overuse of antibiotics. See the newspaper articles cited in nn. 35–39.

45. I found only two studies that compared, in a controlled way, babies born at home with those born in the hospital: Clarke, McGeoch, and Sippe, "Neonatal Infection of the Skin" (n. 41); and P. N. Edmunds et al., "Pathogenic Staphylococci in the Environment of the Newborn Infant," *Brit. Med. J.*, 1955, *1*: 990–94. The babies in both studies were nursed by hospital nurses as part of the domiciliary nursing program; however, as Clarke et al. note (p. 655), "the nasal carrier rates for children born at home were remarkably low, although these children were attended by nurses from a hospital where the nasal carrier rate was high."

46. Campbell, "Cross Infection in the Neo-Natal Nursery" (n. 41).

47. Some of the first investigators to determine this were Clair Isbister, "A Clinical Study of Infections of the Newborn Occurring in a Maternity Hospital over a Six-Month Period," *Med. J. Australia*, September 1951, pp. 386–95; Colbeck, "Extensive Outbreak" (n. 41); Mary Barber, F. G. J. Hayhoe, and J. E. M. Whitehead, "Penicillin-Resistant Staphylococcal Infection in a Maternity Hospital," *Lancet*, 1949, *2*: 1120–25; Phyllis M. Rountree and R. G. H. Barbour, "*Staphylococcus pyogenes* in New-Born Babies in a Maternity Hospital," *Med. J. Australia*, April 1950, pp. 525–28.

desirability of rooming-in in single wards as a general principle, there can be little doubt that, for the new-born infant in a single bed ward, it provides a measure of protection from infection."[48] An American report stated: "Rooming-in facilities will probably be increased on demand from an enlightened public. Hospital construction should anticipate the problem of infection of patients from resistant strains of bacteria by providing larger and more adequately equipped maternity units."[49] These ideals were achieved on a small scale during the period. For example, rooming-in was initiated at the RNS Hospital, where Rountree had discovered the first cases of 80/81 infections in 1954. While one of the prime motivations for initiating the practice was the reduction of cross-infection, another was the promotion of breast-feeding;[50] however, as the seriousness and prevalence of staphylococcal infections declined during the 1960s, so did the practical need for rooming-in. Despite the efforts of phage typers and physicians focused on preventive care, the wide-scale implementation of rooming-in was not realized. It represented the optimal situation from an infection-control perspective, but hospital architecture, among other things, did not support the practice.

The epidemiologic findings of phage typing, together with the practical suggestions made by hospital bacteriologists in light of these findings, helped them to extend their influence beyond the laboratory and onto the wards of the hospital. In their new roles as infection-control experts, they used their scientific investigations to inform decisions about the management of patient care. In many cases, this was done in the context of infection-control committees.

48. Central Health Services Council, Standing Medical Advisory Committee, *Staphylococcal Infections in Hospitals* (London: Ministry of Health, 1959), p. 21.

49. Joint Committee on Staphylococcal Infections, *Control of Staphylococcal Infections in Hospital* (Albany: New York State Department of Health, 1958), p. 23. See also W. Harding leRiche, *A Study on Staphylococcal Infections in the Toronto Western Hospital* (Toronto: Department of Public Health, School of Hygiene, 1958); Campbell, "Cross Infection in the Neo-Natal Nursery" (n. 41); Clarke, McGeoch, and Sippe, "Neonatal Infection of the Skin" (n. 41); Douglas and Knights, "Some Public Health Aspects" (n. 41); Gillespie, Simpson, and Tozer, "Staphylococcal Infection in a Maternity Hospital" (n. 41); A. F. Hardyment, "The Control of Infections in the Newborn," *Can. Med. Assoc. J.*, 1954, *70*: 379–82; Kessler and Scott, "Staphylococcal Infections in Young Infants" (n. 25); Mathew, "Experience with *Staphylococcus* Infections" (n. 41); J. A. Monro and N. P. Markham, "Staphylococcal Infection in Mothers and Infants: Maternal Breast Abscesses and Antecedent Neonatal Sepsis," *Lancet*, 1958, *2*: 186–90; Reimert T. Ravenholt, Priscilla Wright, and Marie Mulhearn, "Epidemiology and Prevention of Nursery-Derived Staphylococcal Disease," *New England J. Med.*, 1957, *257* (17): 789–95; Timbury et al., "*Staphylococcus* Type-80 Epidemic" (n. 25); Wysham et al., "Staphylococcal Infections" (n. 41).

50. Personal communication, Clair Isbister, 31 October 2001.

Infection Control

The beginnings of the field of infection control have been discussed by some of the original participants (no historical papers by nonparticipants have been written), and all agree that the field began in the mid-twentieth century as a response to staphylococcal hospital infections.[51] Harry Dowling has written a comprehensive, American-based book about infection that covers the period from the mid-nineteenth century to the 1970s. Many of the problems and events on which he focuses feature bacteriology and bacteriologists, but because of the wide scope of the book, staphylococcal infections are examined in only three paragraphs. Dowling alludes to the importance of strain identification and differentiation, but he does not discuss how it was done—namely, through phage typing.[52] In general the literature does acknowledge the importance of understanding how infections spread, but it fails to discuss, at any length, how this information was gathered.

Infection control is a field that began earlier in Great Britain and Australia than it did in the United States, and this may be attributed to two factors: First, the most prominent phage typers were British and Australian, and assuming that the use of phage typing stimulated the formation of infection-control committees, then obviously the countries most interested in the technique were most likely to form committees. Second, both Britain and Australia had nationalized health systems, and any solutions to problems encountered at a prominent hospital using phage typing to investigate staphylococcal infections could easily be dealt with at a national level—that is, the results and information gained about infections at one

51. The quality of material regarding the development of hospital infection control is disappointing due to its lack of a wider consideration of the sociological roles played by the various classes of people involved. There is no social history written regarding the field, only haphazard accounts of basic timelines. See Robert I. Wise, Elizabeth A. Ossman, and Dwight R. Littlefield, "Personal Reflections on Nosocomial Staphylococcal Infections and the Development of Hospital Surveillance," *Rev. Infect. Dis.*, 1989, *11*: 1005–19; Christopher E. Laxton, "Infection Control: An Idea Whose Time Has Come," *Amer. J. Infect. Control*, 1997, *25* (1): 34–37; James D. Whitehouse, Daniel J. Sexton, and Kathryn B. Kirkland, "Infection Control: Past, Present, and Future Issues," *Contemp. Therapy*, 1998, *24* (2): 71–77; William E. Scheckler, "Surveillance, Foundation for the Future: A Historical Overview and Evolution of Methodologies," *Amer. J. Infect. Control*, 1997, *25* (2): 106–11; Mary E. LeBlanc and Carol A. Whyman, "Chica-Canada—An Historical Perspective: 1976–1994," *Can. J. Infect. Control*, 1995, *10* (3): 83–88; Elaine Larson, "A Retrospective on Infection Control: Part 1: Nineteenth-Century—Consumed by Fire," *Amer. J. Infect. Control*, 1997, *25* (3): 236–41.

52. Harry F. Dowling, *Fighting Infections* (Cambridge, Mass.: Harvard University Press, 1977).

hospital could, in turn, affect changes in hospitals throughout the country. Phage typing for staphylococci was a British invention created for use in the Public Health Laboratory Service (PHLS), a centralized agency responsible for public health issues throughout the nation. Robert Williams, who was in charge of the staphylococcal reference laboratory at the PHLS, had previously worked in wound infection at the Medical Research Council (MRC) Unit of the Birmingham Accident Hospital, where phage typing had been used since its invention.[53] Similarly in Australia, Rountree founded the staphylococcal reference laboratory at the RPA in 1948, and this laboratory served as the national reference laboratory for both Australia and New Zealand with funding provided by the Department of Health. These countries thus had organized, national systems for dealing with staphylococcal infections already established in the years before the nursery epidemics. Both Colindale and the RPA received infective and epidemic strains from across the country and typed them centrally. The situation seems to have been similar in Canada, with Ottawa serving as the central point for phage distribution throughout the country.[54]

In addition, not many hospital laboratories could immediately take up phage typing, even when faced with problematic staphylococcal infections. Phage typing was (and still is) a complicated technique and is expensive in both financial terms and man-hours. It proved to be difficult to learn, because its procedures require much specialized skill and tacit knowledge. Not only is the technique difficult, but the phages themselves are unstable organisms: they can change rapidly, and must periodically be standardized and calibrated to maintain their sensitivities. A centralized system therefore worked best for distributing the gains of phage typing.

The situation in the United States was markedly different from that in England, Australia, and Canada. The U.S. representative on the International Subcommittee for Phage Typing of Staphylococci was Dr. John E. Blair, bacteriologist of the Hospital for Bone and Joint Diseases in New York. He was the sole phage typer (outside the Army) in that country

53. See E. J. L. Lowbury, "Burn Infection Studies," *J. Hospital Infect.*, 1996, *32*: 167–73.

54. The Canadian situation is more difficult to characterize because phage typing had been used in some seminal studies in the late 1940s, before the formation of the International Subcommittee for Phage Typing of Staphylococci (in 1953). When the Subcommittee was formed, its Canadian representative was not the most prominent phage typer, but Bynoe. For papers on the earlier use of phage typing in Canada, see Colbeck, "Extensive Outbreak" (n. 41). A later report, written by Bynoe, clarifies the very hierarchical structure that phage-typing facilities adopted circa 1960: Bynoe stipulated that Ottawa was to serve as the main central laboratory in charge of all the provincial laboratories, which, in turn, were responsible for all the phage typing done at major hospitals in the larger Canadian cities. Bynoe's report is found in the Murray Papers, MG30, vol. 32, p. 4.

until 1953, yet he had no local, let alone national, responsibility for typing strains.[55] Unlike the laboratories of his British, Australian, and Canadian counterparts, his was not governmentally funded and hence did not function in a public health capacity. When the International Subcommittee was formed in 1953, Blair acted as a source of phages, propagating strains and providing details of procedures to other American bacteriologists interested in phage typing—but he still typed only strains from within his own hospital. For example, he shared his strains and knowledge with the bacteriologists Drs. Robert Wise and Vernon Knight in 1953, who in turn organized phage-typing facilities at the University of Minnesota and the Cornell Medical Center respectively—where, again, phage typing was done only locally, without an organized network through which to share results and responsibilities.[56] Thomas Shaffer, the American researcher who first discovered 80/81 in the United States, also typed his strains locally in a laboratory at Ohio State University.[57] The localized rather than national organization of phage typing in the United States probably accounted for the fact that Shaffer was using uncalibrated phages, thus confusing his results.[58]

Due partly to this distinction between national and local responsibility for phage typing, therefore, Britain and Australia organized infection-control committees before the United States. The formation of these committees was stipulated in the newly published infection-control manuals, which themselves were the products of government organizations. For example, Rountree and Isbister, together with an obstetrician, a public servant, and a physician, wrote the first manual regarding the control of hospital staphylococcal infection (specific to the nursery) in 1956.[59] The

55. For early phage-typing work in the United States, see John E. Blair and Miriam Carr, "The Bacteriophage Typing of Staphylococci," *J. Infect. Dis.*, 1953, *93* (1): 1–13. For Army-based phage-typing work, see Fusillo, Roerig, and Ernst, "Phage-Typing the Antibiotic-Resistant Staphylococci: IV" (n. 28); Capt. Joseph Metzger et al., "Phage Typing of Antibiotic-Resistant Staphylococci: III. Infection, Crossinfection, and Superinfection," *New England J. Med.*, 1954, *250*: 1030–33.

56. In the United States, various research centers related to hospital infection and based on phage typing were established throughout the country: in New York, Chicago, Boston, Philadelphia, Columbus, Cleveland, Minneapolis, and San Francisco. See Wise, Ossman, and Littlefield, "Personal Reflections" (n. 51).

57. Shaffer did not indicate where the strains were typed in his original article on the epidemics, but did mention the Ohio State Laboratory in a 1956 letter to the editor: Shaffer, "Epidemics of Micrococcic Infections" (n. 27).

58. See n. 30.

59. The manual was the first of its kind in Australia, and probably in the world (this assertion is based on the publication dates of the other manuals that I have found).

pamphlet was commissioned by the Australian NH&MRC, and it drew on the research done by Isbister at the RNS, both before and after her collaboration with Rountree. The production of this booklet prompted some of Rountree's Canadian and U.S. colleagues to request copies so that they could undertake similar projects.[60] The booklet was distributed by the NH&MRC to all maternity hospitals in Australia. Its foreword reads:

> The Council felt that a booklet of this type was desirable because the magnitude of the problem of staphylococcal infections in maternity hospitals is not realized by the medical and nursing professions generally and the problem of control is not yet solved. . . . neither infection in the newborn nor breast abscess is notifiable and . . . collection of information has therefore been difficult.[61]

The sponsorship of such booklets by the NH&MRC in Australia and the MRC in England (in 1959) reinforces the emerging role of hospital bacteriologists as infection-control experts, both in the context of their own hospitals and also as agents of the government, to be called on in times of crisis. Notification of staphylococcal infections to public health departments was one recurring theme among bacteriologists in this period, and especially among those in the United States. Many of the research articles written in this period called for the formation of cross-infection committees in hospitals and outlined how they might work—for example, by producing hospital-infection-control booklets containing guidelines for the standardization of procedures.[62]

The Americans finally began to move toward a nationalized system for studying staphylococcal infections when the Communicable Disease Center (CDC—now the Centers for Disease Control and Prevention) was alerted to an epidemic in the summer of 1956. Reimert Ravenholt, an epidemiologist working at the Seattle–King County Department of Public Health, contacted the CDC with what he thought was the "most important public health communicable disease problem in the United States at the

60. Rountree to Shaffer, 12 October 1956, Rountree Papers, MLMSS 6484.

61. Phyllis M. Rountree, J. Sinclair [Clair] Isbister, Lorimer Dods, C. E. Cook, and Bruce T. Mayes, *Staphylococcal Infections in Maternity Hospitals: Report by the Special Committee Appointed by the National Health and Medical Research Council to Investigate Staphylococcal Infections in Maternity Hospitals and to Suggest Measures of Control* (Canberra: National Health and Medical Research Council, 1956), foreword (unpaginated).

62. Contemporary articles that made these suggestions include Duthie, "Generalized Staphylococcal Epidemics" (n. 25); Shaffer et al., "Infections in Newborn Infants: II" (n. 25); Fekety et al., "Control of an Outbreak of Staphylococcal Infections" (n. 25); Murray, McDaniel, and Reed, "Evaluation of the Phone Survey" (n. 25); American Academy of Pediatrics, "Staphylococcic Infections in the Newborn," *JAMA*, 1958, *166*: 1900; Timbury et al., "*Staphylococcus* Type-80 Epidemic" (n. 25); Smith, "Role of a Chronic Carrier" (n. 25).

time—Staphylococcal disease in hospital."[63] The CDC, in turn, sent two officers to Seattle to track the infections using the new method of phage typing.[64] The CDC's involvement in this investigation represented the first national, organized approach to studying hospital infections in the United States.

The publication of infection-control booklets accelerated during this time and featured *Staphylococcus* prominently.[65] The recommendations made in these booklets included the need for bacteriologists to be key members of infection committees in hospitals, along with an administrator, a senior clinician, a nursing representative, and "someone from housekeeping."[66] The interdisciplinary make-up of these committees was key in assuring that they could adequately deal with a hospital-wide problem in an organized manner. As stipulated at a 1963 symposium on hospital infection, "the infections committee . . . should be representative of all the disciplines in the hospital."[67] In Great Britain, a 1959 report from the Ministry of Health suggested that one person on the committee be made the "Control of Infection Officer," and that "the hospital bacteriologist is often the person of choice."[68] In addition, the booklets repeatedly stressed the need to create notification procedures for staphylococcal infection, normally through the infection-control committee. They also

63. Neal Nathanson and E. Russell Alexander, "Infectious Disease Epidemiology," *Amer. J. Epidemiol.*, 1996, *144* (8): s34–s38, on p. s36. Ravenholt was dealing with an endemic incidence of staphylococcal infection in the Seattle, Washington, area: see Reimert T. Ravenholt and G. D. La Veck, "Staphylococcal Disease—An Obstetric, Pediatric, and Community Problem," *Amer. J. Pub. Health*, 1957, *46*: 1287–96; Ravenholt, Wright, and Mulhearn, "Epidemiology and Prevention" (n. 49).

64. Nathanson and Alexander, "Infectious Disease Epidemiology" (n. 63). The officers obtained their typing phages from John Blair, the American representative on the International Subcommittee for Phage Typing of Staphylococci.

65. Several such booklets, in addition to Rountree's 1956 report, were found in the Murray Papers, MG 30, B91, 31, 28-10, 28-11, and 28-12: Central Health Services Council and Standing Medical Advisory Committee, *Staphylococcal Infections in Hospitals* (n. 48); Joint Committee on Staphylococcal Infections, *Control of Staphylococcal Infections in Hospitals* (n. 49); leRiche, *Study on Staphylococcal Infections in the Toronto Western Hospital* (n. 49); and the Cross Infection in Hospitals Committee of the Medical Research Council, *The Control of Cross Infection in Hospital* (London: Privy Council Medical Research Council, 1951). This last report does not deal with staphylococcal infection at great length, while the others feature it predominantly.

66. Joint Committee on Staphylococcal Infections, *Control of Staphylococcal Infections in Hospitals* (n. 49), p. 4.

67. Philip S. Brachman, "Surveillance of Hospital-Associated Infections," in Williams and Shooter, *Infection in Hospitals* (n. 7), pp. 329–38, on p. 329.

68. Central Health Services Council, and Standing Medical Advisory Committee, *Staphylococcal Infections in Hospitals* (n. 48), p. 26.

discussed the use of phage typing as a useful epidemiologic tool; however, they stressed that because few facilities existed for this type of work, and because of the labor- and capital-intensive nature of the technique, it could not be standard practice except in cases of epidemic.[69]

The Medical Board of the RPA formed a cross-infection committee in 1958, with Rountree and Dr. Edgar Thomson, the head bacteriologist, as key members. Other members were the professor of surgery, the senior surgeon, and the superintendent. In her capacity as a member of this committee, Rountree was also responsible for lecturing to both lay and medical operating-room staff regarding issues of cross-infection.[70]

The formation of infection-control committees, and the establishment of the field of hospital infection control, paradoxically preceded a worldwide decline in the number and severity of staphylococcal infections, even those caused by the especially virulent strain 80/81. This strain has proved to be the first and last great epidemic strain of *Staphylococcus*—one that could actually cause infection in otherwise healthy tissue and spread rampantly throughout the general population. The legacy of this strain lives on, however, in the field of infection control.

The Origins and Eclipse of 80/81, and a New Wonder Drug

Rountree was the first to identify strain 80/81, but whether it actually originated in Australia remains unknown. In 1958, at the height of the pandemic, it was even suggested that it was the strain responsible for the Bundaberg disaster of 1928, which was the first incidence of mass death due to *Staphylococcus* in the twentieth century (and coincidentally occurred in the year of penicillin's discovery). Bundaberg was an Australian tragedy in which twelve children died after inoculation with a *Staphylococcus*-contaminated batch of diphtheria toxin and antitoxin.[71] Had the Bundaberg strain been shown to be 80/81, it would have been an important link in the epidemiology of the strain—but this proved

69. Ibid., p. 8; Joint Committee on Staphylococcal Infections, *Control of Staphylococcal Infections in Hospitals* (n. 49), p. 30.

70. Copies of Rountree's lectures can be found in Rountree Papers, MLMSS 6482, box 7, folder 7/2, "Student Lectures-notes."

71. C. H. Kellaway, P. MacCallum, and A. H. Tebbutt, "The Fatalities at Bundaberg," *Med. J. Australia*, July 1928, pp. 2–30. The episode had lasting effects on the immunization program in Australia: see Claire Hooker, "Diphtheria, Immunization and the Bundaberg Tragedy: A Study of Public Health in Australia," *Health & Hist.*, 2000, *2*: 52–78.

not to be the case.[72] The origin of the strain has always been a mystery to those in the field, and there has been much discussion regarding the probability of a de novo appearance of the strain, seemingly simultaneously, in Canada and Australia.

The origin of 80/81 is nearly as mysterious as its "eclipse" in the mid-1960s. More-optimistic accounts have attributed this eclipse to a greater awareness of infection control brought about by the newly formed infection-control committees.[73] Hospital workers certainly became increasingly aware of aseptic methods and of the more rational use of antibiotics during the years of the nursery epidemics—but whether this increased knowledge and better practice made much of a difference is debatable, for the actual carrier rates of *Staphylococcus* found in hospitals and on patients remained constant from the 1950s to the 1970s.[74] More cynically, many of those intimately involved in the field have attributed the eclipse of 80/81 to a random fluctuation.[75] It is thought that the strain was a somewhat "freak occurrence," and that once it had run its natural course, no other strain as virulent existed to take its place. This could have occurred in the context of some unknown ecological force in the habitat of staphylococcal strains. Strain 80/81 was certainly displaced by other, less virulent, strains during the 1960s and 1970s (e.g., strains 84 and 85).[76] As Rountree pointed out in a 1962 article, staphylococcal infections are dependent on two factors, virulence and transmissibility, and the importance of these two variables fluctuates in the presence of other strains.[77] In addition to this, strain 80/81 was unique and unpredictable in its behavior, so its disappearance was presumably difficult to quantify. Regardless of the reasons for the eclipse, one thing is certain: ideas about hospital infection had certainly changed as a result of the proliferation of dangerous staphylococcal infections during the mid-1950s.

72. Stuart Mudd to Rountree, 20 November 1958; Rountree to Mudd, 26 November 1958, Rountree Papers, MLMSS 6482.

73. None of the papers I have read seriously puts forth this idea. If true, this would be wonderful—but in reality, 80/81 was nearly unstoppable.

74. For example, see Wise, Ossman, and Littlefield, "Personal Reflections" (n. 51).

75. For comments on this, see Phyllis M. Rountree, "History of Staphylococcal Infection in Australia," *Med. J. Australia*, December 1978, pp. 543–46; Gordon and Barker, *Phyllis Margaret Rountree* (n. 6), p. 23; Wise, Ossman, and Littlefield, "Personal Reflections" (n. 51); Parker, "Significance of Phage-Typing Patterns" (n. 8).

76. Parker, "Significance of Phage-Typing Patterns" (n. 8). See also Rountree, "History of Staphylococcal Infection" (n. 75); Gordon and Barker, *Phyllis Margaret Rountree* (n. 6), p. 25.

77. Phyllis M. Rountree, "The Origin and Spread of Virulent Staphylococci," *Recent Prog. Microbiol.*, 1962, *8*: 561–69.

Coincidentally, the eclipse of 80/81 occurred at just the time when the next great wonder drug, methicillin, was discovered. This new drug was the product of research performed by Ernst Chain, who had earlier been awarded the Nobel Prize in Physiology or Medicine for his work with penicillin.[78] Methicillin is a synthetic antibiotic designed specifically to combat the action of penicillinase, an enzyme produced by staphylococci that destroys the beta-lactam ring of penicillin, thereby making the drug useless. At the time of its synthesis in 1960, methicillin was highly praised as an example of the thoughtful and methodological processes of science conquering the staphylococci's natural ability to produce penicillinase.[79] It marked a new paradigm for chemotherapy: that of purpose-built, semi- or wholly synthetic antibiotics.

Excessive optimism based on this new scientific conquest was rampant. An extreme and startling example of this, in relation to nursery infections, is found in an editorial of the *Canadian Medical Association Journal* published in November 1960. This editorial, written by a physician, advocated the widespread and "deliberate introduction into the atmosphere of an antibiotic [methicillin] lethal to all staphylococci."[80] The author expressed hope that the new penicillinase-resistant, synthetic antibiotics could be the drugs of choice. Such comments indicate the opposition faced by bacteriologists at the time with regard to the prevention of antibiotic misuse. A later sentence in this editorial proved to be prophetic: "It remains to be seen whether or not strains of staphylococci resistant to even these new penicillinase-insensitive synthetic penicillins will yet emerge";[81] one year later, resistance to methicillin was in fact observed.[82]

Apart from the rapid development of resistance to methicillin by some strains of *Staphylococcus*, the drug was extremely useful in treating infections that did not respond to other antibiotics. It seemed that the optimistic promises made when penicillin was discovered would finally be fulfilled with methicillin: the war on *Staphylococcus* had been won. However, this was not to be the case. Since the mid-1970s a new problem has been emerging in hospitals and communities: methicillin-resistant *Staphylococcus aureus* (MRSA). MRSA strains are increasingly infecting more and more hospital

78. Chain shared the prize with Alexander Fleming and Howard Florey in 1945.

79. E. B. Chain, "Conquest of the Resistant *Staphylococcus* by New Penicillins," *New Scientist*, 29 September 1960, pp. 838–40.

80. Editorial, "Trouble in the Nursery" (n. 25), p. 1112.

81. Ibid., p. 1113.

82. M. Patricia Jevons, "Celbenin"-Resistant Staphylococci," *Brit. Med. J.*, January 1961, p. 124.

patients and members of the general public worldwide, often with fatal outcomes.[83] Infection-control experts are again on the job, as it were, to investigate and try to control these new outbreaks of infection, and their message has not changed: the best way to stop staphylococcal infections is to maintain strict aseptic techniques in hospitals and to use antibiotics sparingly and with care, thereby avoiding the development of resistant strains in the first place.[84]

Although the field of infection control emerged out of a pressing need to understand and halt staphylococcal hospital infections during the 1950s, it has expanded broadly beyond this initial aim. In recent years, infection-control experts have been on the forefront of understanding AIDS and antibiotic-resistant tubercular infections, and other bacterial and viral infections that affect hospital patients. Also, in light of the continuing presence of MRSA infections in hospitals and communities, the future will be interesting for both infection-control experts and *Staphylococcus*.

With regard to the nursery epidemics, in spite of the best efforts of phage typers to promote nonpharmacological solutions, in the end many who were involved in the events described here agreed that the infections were most successfully stopped by hexachlorophene, an antiseptic that was used in solution to "wash" the skin of all newborns. Rountree summed this up in a 1978 review article of staphylococcal hospital infections: "control of these outbreaks by a variety of methods was only partially successful, until the practice of washing all newborn babies with an emulsion containing hexachlorophene was instituted; and this brought about an immediate fall in sepsis rates."[85] Hexachlorophene was first suggested as a compound active against *Staphylococcus*, and hence useful for controlling nursery infections, in 1952.[86] However, washing newborns' skin was not a new practice at the time. From the beginning of the twentieth century,

83. Henry F. Chambers, "The Changing Epidemiology of *Staphylococcus aureus*?" *Emerg. Infect. Dis.*, 2001, *7* (2): 178–82.

84. One thing that has changed in the past forty years is that phage typing is increasingly becoming outdated as bacteriologists continue to develop molecular techniques for differentiating strains of staphylococci. See J. Stepan, R. Rantucek, and J. Doskar, "Molecular Diagnostics of Clinically Important Staphylococci," *Folia Microbiologica*, 2004, *49* (4): 353–86; R. R. Marples and V. T. Rosdahl, "International Quality Control of Phage Typing of *Staphylococcus aureus*: International Union of Microbial Societies Subcommittee," *J. Med. Microbiol.*, 1997, *46* (6): 511–16.

85. Rountree, "History of Staphylococcal Infection" (n. 75), p. 544.

86. C. D. Farquharson et al., "Control of Staphylococcal Skin Infections in [the] Nursery," *Can. Med. Assoc. J.*, 1952, *67*: 247–49.

compounds such as ammoniated-mercury ointment, mercuric chloride solution, or copper oleate had been used.[87]

The use of a simple antiseptic process to halt the epidemics seems anticlimactic to the story of nursery epidemics, particularly compared to more "high tech" solutions. However, the most important aspect of the situation is perhaps not how the infections were stopped but how they were studied, and the resultant linkages between science and practice. The use of phage typing gave hospital personnel a clear view of how the infections spread and provided a credible method to support the emerging field of hospital infection control. Bacteriologists and phage typers, through their persistent efforts to determine the epidemiology of the staphylococcal nursery epidemics, provided much of the initial theoretical and practical support for the creation of the infection-control specialist.

Conclusion

The discovery of the 80/81 strain of *Staphylococcus*, responsible for worldwide epidemics of nursery infections in the mid-1950s, was an important event for phage typers, for it gave them opportunities to prove the efficacy of their new tool. Strain 80/81 proved to be the most troublesome strain of this bacterium to date. It had the ability to cause infection and death in otherwise healthy people, most critically in newborn babies. Also, it was the first hospital strain to migrate to the general community.

The epidemiologic results of phage typing were vital to the emerging field of infection control, a fact that has been overlooked by historians. Bacteriologists became key members of this field, and their status was raised from mere technician to infection-control expert, a role that assumed more responsibility for the management of patient care. They were invited to be members of cross-infection committees and were coauthors of infection-control manuals in which the procedures and practices for dealing with hospital infection were outlined. The field of infection control originated in Great Britain and Australia, where it was supported by nationalized systems of health care.

Strain 80/81 disappeared in the mid-1960s, but it left an enduring legacy. The virulence and pervasiveness of 80/81 united bacteriologists,

87. Horace M. Gezon, Donovan J. Thompson, Kenneth D. Rogers, Theodore F. Hatch, and Paul M. Taylor, "Hexachlorophene Bathing in Early Infancy," *New England J. Med.*, 1964, *270* (8): 379–86; Louis Gluck and Harrison F. Wood, "Staphylococcal Colonization in Newborn Infants with and without Antiseptic Skin Care," ibid., 1963, *268* (23): 1265–68.

clinicians, nurses, and administrators in interdisciplinary measures aimed at stopping the infections caused by it. Bacteriologists contributed their expert epidemiologic knowledge and in doing so established themselves as experts on infection control, a role that they continue to hold.

KATHRYN HILLIER is both an Honorary Associate in the Unit for History and Philosophy of Science, and Research Assistant in the School of Philosophical and Historical Inquiry at the University of Sydney, Australia. She holds degrees in chemistry, education, and history of medicine. She is currently researching issues related to infection control and phage, and is also working on a project looking at Australia's involvement with chemical and biological weapons, which is supported by an Australian Research Council grant. Her address is: Unit for History and Philosophy of Science, The University of Sydney, Carslaw Building (F07), NSW 2006, Australia (e-mail: k.hillier@science.usyd.edu.au).