MEDICAL PROGRESS

STAPHYLOCOCCAL INFECTIONS IN HOSPITALS (Concluded)*

Recent Developments in Epidemiologic and Laboratory Investigation

André J. Nahmias, M.D., M.A., M.P.H.,† and Theodore C. Eickhoff, M.D.‡

ATLANTA, GEORGIA

The Environment

The environment may be broadly defined as the totality of inanimate objects with which people may come in direct or indirect contact. Contamination of the environment with bacteria, and more specifically *Staphylococcus aureus,* has been found to occur in virtually every area of the hospital. In general patient-care areas, *Staph. aureus* has been recovered from such items as clothes, mattresses, pillows, blankets, laundry, curtains, walls, floors, bed frames, bassinets and cleaning equipment. Common articles of personal hygiene, such as combs, toothbrushes and razors, may also be heavily contaminated. An ordinary bar of soap, without disinfectant additives such as hexachlorophene, may permit a heavy growth of cocci and other organisms, particularly if the soap remains in a moist state.[231] Walter et al.[232] recently called attention to the common bedside carafe as frequently being a heavily contaminated object and pointed out several other cycles of contamination within the hospital.[212] Others have brought out the fact that articles used in hospital-ward practice, commonly regarded as sterile as a result of steam sterilization, upon careful examination were found to be contaminated.[233]

Contamination by *Staph. aureus* outside hospitals is believed to be less widespread,[211] although no comparative studies of a broad coverage of items in and out of hospitals have been made. It is quite conceivable that heavy contamination might occur in the homes of infected persons who may be discharging staphylococci. Walter[212] and Colbeck[211] have found that in rooms occupied by patients who were carriers or were suffering from staphylococcal disease, the bath, toilet seat and bedside table sometimes showed heavy contamination with the same phage type of staphylococcus as that harbored by the patient.

Methods of sampling of fomites using semiquantitative technics have been reviewed by Hall and Decker.[234] In addition, Foster[235] has improvised a semiquantitative surface-sampling procedure for floors or other surfaces using slabs of agar reinforced with gauze. He was able to use this method to measure contamination of the environment by individual patients, and to investigate crossinfection and the effect of ward cleaning.

The determination of aerial contamination with staphylococci was made possible by the various methods of air sampling. Since the development by Wells, in 1933, of the first air centrifuge for counting the number of contaminated particles in air, many different types of aerosol samplers have been produced.[234] A recent review[236] describes the various types, as well as the various problems, of air samplers. Blowers and Wallace[237] stress the value of the simple agar sedimentation plate, which provides information on fall out not obtainable by the volumetric type of sampler. They also review some of the uses of air-sampling methods to evaluate aerial contamination in operating rooms in relation to sepsis, ascribing a great deal of postoperative sepsis to a slit-sampler count of 20 to 50 particles per cubic foot of operating-room air, with a ratio of 1:20 *Staph. aureus* colonies to the general colony count, and the sedimentation plate collecting about 10 particles per square foot per minute, or about 0.5 particles of *Staph. aureus* per square foot per minute. Less sepsis arose postoperatively if the corresponding figures were 1 or 2 particles per cubic foot of air, a ratio of 1 *Staph. aureus* to 100 colonies, a sedimentation rate of 0.5 particles, or 0.005 *Staph. aureus* per square foot per minute. However, the authors could not commit themselves on definite limits of safety for the air in operating rooms.

Air-sampling studies in operating rooms have revealed a consistent pattern of aerial contamination.[237,238] Low counts were observed in an empty room, rising to somewhat higher levels as the nurses prepared the room before surgery. Air counts then rose markedly as the patient and surgical staff entered the room. During the operation itself, counts fluctuated at moderate levels, often varying with the amount of activity in the room. Another sharp rise was frequently observed when the patient and surgeons left the room, followed by a quick return to low levels. Later, during the "cleaning" of the room, another sharp rise in aerial contamination was commonly noted.

Frequently, in spite of the many precautions taken to ensure relative sterility in operating rooms, little attention is devoted to the patient and the manner

*From the Communicable Disease Center, Public Health Service, United States Department of Health, Education, and Welfare.

†Senior assistant resident, Pediatric Service, Boston City Hospital; formerly, epidemic intelligence service officer, Epidemiology Branch, Communicable Disease Center.

‡Resident in medicine, Second and Fourth (Harvard) Medical Services, Boston City Hospital; formerly, epidemic intelligence service officer, Epidemiology Branch, Communicable Disease Center.

in which he is brought into the room. Too frequently he is brought in without prior bath, without mask or cap and covered by sheets and blankets that may be highly contaminated. Excessive movement of personnel in operating rooms — such as random entry and exit of nonessential personnel — and excessive talking are likely to contribute air-borne contaminants, which may readily settle into the operative wound. Blowers and Wallace[237] demonstrated that with reduced activity, exhaust ventilation and the doors remaining closed, the bacterial count was decreased. It was reduced even further when positive-pressure ventilation was used.

Dirty laundry has been shown[239] to contaminate the air in laundry chutes heavily. It has also been demonstrated that such air frequently enters the general hospital circulation when chute doors are opened, resulting in significant contamination of hospital-corridor air.

The epidemiologic significance of environmental contamination has been difficult to establish. All routes of transmission except that of direct contact pass, of necessity, through the environment in one way or another.[234] The first such route is by means of droplets, which are propelled by coughs or sneezes at high speed from person to person. The organisms remain in their original body fluids, a fact that has caused some workers to classify this droplet route as "direct." Another possible route is through droplet nuclei, in which the organisms remain in the air after evaporation of the body fluids. It is mainly these suspended particles in air that are measured by air-sampling devices.

There is little question that all three routes — droplets, droplet nuclei and direct contact — can serve to contaminate the fomites in the environment. The crucial point is whether the staphylococci found in the environment are less infective, or perhaps not at all infective, as compared to those found in human hosts.

Colbeck[211] reported on experiments in rabbits, in an attempt to determine whether there was a loss of pathogenicity of staphylococci dried on textiles. Woolen treads, previously autoclaved, were dipped in an overnight culture of a staphylococcus strain, phage Type 81, known to cause abscesses in rabbits when 100,000 or more organisms were injected subcutaneously. These threads were then dried at room temperature for one, two, six, seven and fourteen days, viable counts made, and the dried threads sutured into the backs of rabbits. In this fashion it was found that, despite a moderate loss in viable count of the organisms, abscesses were induced in all rabbits tested up to fourteen days.

Maltman et al.[240] also reported on the effects of desiccation on *Staph. aureus* under conditions designed to mimic natural air drying. Cells that survived prolonged periods of drying were found to differ from fresh cells in their greater susceptibility to environmental changes, such as distilled water, saline solution, broth and human serum. The longer lag period of the dried cells and their slower rate of coagulase production was also demonstrated. In vivo studies[241] also revealed a decreased virulence for mice by intramuscular, intravenous and intracerebral methods of testing. These workers concluded that the infective potential of environmental staphylococci was probably dependent to a large degree on the duration of their residence in the environment.

In another series of experiments, Colbeck[211] was able to relate the pathogenicity of dried material to the number of surviving staphylococci present. The need for the presence of a minimum number of staphylococci to induce the formation of lesions has been noted in the experiments in volunteers conducted by Elek and Conen.[84] This might also help to explain the observation that, although viable staphylococci can be recovered from many operative wounds at the time of closure,[242] comparatively few clinical infections actually occur. However, a multitude of other factors related to the host, the surgical technic, anesthesia, antibiotics and so forth may be involved in the development of a wound infection, granting contamination with staphylococci.

A closely related problem in assessing the true significance of environmental contamination is that most investigators measure the number of viable organisms recovered rather than clinical disease caused thereby. To measure clinical disease as an end point and evaluate the effect of varying one factor in the environment in a controlled situation requires periods of observation that are extremely long, to say nothing of the difficulty of varying only one of the many factors in the environment and among personnel. Conditions within different hospitals or the same hospital may be so variable that a factor of great significance in one location may be relatively unimportant in another. Such considerations may help explain the widely divergent differences in results and interpretation reported in the literature.

Thus, for example, several conflicting reports on the importance of aerial contamination in the operating room have appeared. Blowers et al.[243] described a reduction in wound sepsis from 11 per cent to 5 per cent of all operations in a thoracic surgical unit by improving air ventilation in the operating room. However, they admitted that this could not be conclusive evidence, since improved conditions and technics within the operating room and hospital were simultaneously introduced. Shooter and his associates[244] reduced the frequency of sepsis by reducing the number of bacteria in the air, without making any other apparent changes. Later, however, after a long study of staphylococci in a surgical unit, it was reported[81] that several waves of aerial contamination of the ward with different strains of *Staph. aureus* occurred but were not necessarily related to the incidence of sepsis. Again, Kinmonth and his coworkers[245] stated that a reduction in aerial contamination failed to decrease the rates of postoperative sepsis and observed that reduction of the bacterial content of the operating-room air, although desirable as a general principle, is unlikely in itself to eliminate infections.

Similarly, in the nursery for newborn infants, the importance of aerial contamination in the spread of infection has been controversial. Wysham[9] and other workers[160] have considered the aerial mode of spread to be important. Indeed, Eichenwald[185] found that certain infants, typically those whose nasal mucosae yielded viral agents, dispersed such vast numbers of staphylococci into their environment that he termed them "cloud babies." Others,[229,246] however, have held that direct person-to-person transmission appeared to be of greater importance than the aerial route. Gezon et al.[174] found not only that aerial contamination in a nursery for newborn infants was minimal but also that the use of measures designed to increase asepsis and decrease crowding of nursery space had no appreciable effect on the incidence of either the staphylococcal carrier state or infection in newborn infants. Again, conflicting evidence exists regarding the value of disinfection of bedding.[205,247,248]

Chemical disinfectants have long been a part of routine hospital housekeeping; to achieve maximal effectiveness, they must be used regularly, systematically and thoroughly.[249] A great and confusing variety of such agents are commercially available. These chemical agents fall into four main groups: quaternary ammonium ion agents; phenolics; alcoholics; and iodophors. Advantages and disadvantages of these various groups have been reviewed by several authorities.[250-253]

Gaseous sterilization is one of the newer advances in this field. Ethylene oxide[254-256] now offers an effective, safe and versatile agent for the sterilization of objects that may be injured by steam sterilization, such as blankets, mattresses, anesthetic and endoscopic equipment. In addition, beta-propiolactone is being investigated as an agent for gaseous sterilization.[257]

The disposition of heavily contaminated material such as dressings, wound drainage and sputum in sealed containers is part of modern hospital housekeeping. Similarly, heavily contaminated laundry and instruments should be sterilized before re-entering the normal laundry and central supply channels. Floor-cleaning and dust-control devices must be used with care. Opinions on the use of vacuum cleaners are divided, although Allen[258] has presented evidence of the effectiveness of at least one type of vacuum cleaner.

In operating theaters the problem of environmental control is magnified by the complexity of modern surgery, the technical equipment necessary and the number of people who are required to participate in the operation, as well as the frequent visitors and observers. Troublesome contamination has been found linked to many of the popular operating-room practices and technics. For example, anesthetic equipment is often difficult to sterilize adequately. Sterile gowns and drapes, after becoming sufficiently moist in use, present little barrier to the passage of micro-organisms.[259] Standard cotton-gauze surgical masks have been noted for their inefficiency as barriers to the passage of micro-organisms, particularly when they have become slightly moist, as occurs after ten to twenty minutes of use.[260] Penikett and Gorrill[261] demonstrated that 16 per cent of standard surgical rubber gloves used in a neurosurgical unit had been punctured by the end of an operative procedure. Casey et al.,[262] as well as Adams and his associates,[260] have shown that the shoes commonly worn in operating theaters are among the most highly contaminated objects to be found.

With such a multiplicity of possible routes of transmission there have been understandably few attempts to evaluate the significance of controlling any one factor. In general, recent studies of the control of postoperative wound infections have properly emphasized a multifactor approach to the control of environmental contamination.[248,260,263] Factors that have been particularly stressed by these investigators include strict attention to aseptic technics, placing the patient on the operating table outside the operating room proper, reduction of excessive talking and movement in the operating room, forbidding the frequent random entry and exit of nonessential personnel, proper gowning and masking of everyone entering the operating room and frequent changing of face masks. Adams et al.,[260] in particular, have stressed the importance of proper attire in operating theaters. A fitted filter sterilizable mask was developed and said to have a 98 per cent efficiency for periods up to five hours. In addition, Browne[220] developed a mask that was effective in stopping infections associated with a nasal carrier.

Positive pressuring of operating-room air is now a widely accepted technic of ensuring the delivery of clean, nearly sterile air to operating rooms and of reducing the possibility of air-borne contaminants entering the room from outside corridors. Air-study technics, as described above, have their greatest practical usefulness in checking that such contaminated air is not gaining access to operating rooms or to wards containing patients at special risk.[264] Walter[201,212] and Fredette[265] have pointed out that, although modern air-conditioning and filtration systems permit the delivery of nearly sterile air to operating rooms, inadequate maintenance may result in marked loss of efficiency. The value of ultraviolet light in operating rooms, enthusiastically pioneered in this country by Hart[266] more than twenty years ago, has not yet been confirmed by other workers. A co-operative double-blind study under the sponsorship of the National Research Council is currently in progress among 5 university-affiliated hospitals. It is hoped to provide a critical evaluation of the effect of ultraviolet light.

The American Academy of Pediatrics has laid down careful standards for the control of environmental contamination within nurseries.[267,268] Canadian investigators[269] recently evaluated infant-nursing technics in several hospitals and identified three factors that appeared to affect the incidence of staphylococcal infections: whether the babies were transferred in and out of the nursery; whether they were bathed; and whether the personnel washed their hands before handling each infant. A somewhat differently oriented evaluation of several hospital nurseries in the United States[270] emphasized the variety of practices followed by these hospitals and the need for more basic knowledge on the utility of certain commonly accepted practices.

Certain other control measures have been used in hospitals to prevent staphylococcal nursery outbreaks. A technic occasionally advocated and in use in certain hospitals is continuous rooming-in. This practice does away with the routine nursery altogether. In at least 1 reported outbreak[13] compulsory rooming-in, which broke the infant-to-infant cycle of transmission, was the technic that was finally successful in halting an epidemic, after other means had been only partially successful.

Another technic recommended by the American Academy of Pediatrics is the use of "rotation nurseries." This consists in the division of a single large nursery into 3 or 4 smaller units, with independent ventilating systems and wash basins. The nurseries are then filled in rotation, each with infants born within a maximum interval of forty-eight hours from oldest to youngest. As one nursery is filled, it is "closed," and the next one "opened." Each nursery is then completely emptied and cleaned after use by each group of infants.

The possible colonization of babies within twenty-four to forty-eight hours, as demonstrated by several investigators,[187,206] raises doubts of the value of early discharge of infants from the nursery. Indeed, in the outbreak reported by Farrer et al.[13] this technic was only partially successful. Further references on the environmental aspects of staphylococcal disease can be found in a recent Public Health Service publication.[271] It can be concluded, however, that much more study is necessary before one can fully assess the relative importance of this route of transmission and the most effective methods of control.

The Community

In a real sense, the community is the ultimate target of the problem of hospital staphylococcal cross-infection and must inevitably bear its total impact. The most obvious impact on the community is measured in terms of spread of staphylococci from the relatively restricted hospital environment into the broad environment of home, school, job and social circle. This occurs daily — as often as patients are discharged and employees go home. One is forced to assume a constant and dynamic state of bacteriologic interchange between hospital and community. That this, in fact, occurs has been amply demonstrated.[8,10-12,63,65,272-280]

Schaffer[62] followed a group of 20 families for eighteen months after the newborn infant, suffering from cutaneous staphylococcal lesions due to an epidemic phage type (80/81), was taken home from the hospital. In 9 of the 20 families followed, 1 or more members of the household still carried the identical epidemic strain in the nasopharynx after eighteen months. In virtually every family there was a history of recurrent staphylococcal lesions in various members.

Wentworth et al.[65] studied 1287 families of infants born during a nursery epidemic of three months' duration. After a follow-up period of one to five months they found that suppurative disease occurred in 45.1 per cent of families of infants who had such disease before or after hospital discharge. Only 9.5 per cent of families in which the infant did not acquire lesions had suppurative illness.

In a more recent study Klein[277] demonstrated an incidence of 12.6 per cent among family contacts of infants in whom lesions had developed during an epidemic. In contrast, only 1.3 per cent of family contacts of infants who were not infected during that period and 1.9 per cent of family contacts of infants born in the postepidemic period gave a history of staphylococcal infections. In addition, he showed that suppurative disease in infants may persist for over a year. Recently, Hurst and Grossman[278] reported on a survey of 94 families into which infants were born during an outbreak of impetigo due to 80/81 strains sixteen months earlier. They found 28 per cent of the infants, 13 per cent of the mothers, 2 per cent of the fathers and 14 per cent of the siblings to be carriers of the 80/81 or 52/52A/80/81 strains. Actual infections were found to have occurred in 44 per cent of the infants, 21 per cent of the mothers, 12 per cent of the fathers and 12 per cent of the siblings. In all, it appeared that the nursery staphylococcus had become disseminated among 65 per cent of families in which infants were born during the outbreak.

Such experiences are by no means limited to families of newborn infants, but occur also among families of medical and surgical patients who may bring home a "hospital" staphylococcus. Once the patients are outside the hospital, familial recurrence and community spread are the rule. Such intrafamilial spread of staphylococci is well illustrated by the results of a seven-year follow-up study of 17 infected families by Roodyn.[279] In 11 of these 17 families, infection was spread from one person to another in the same household. In 2 of the families, strains of staphylococci of similar phage types were noted to remain with the respective families for over six years. In 6 of the 17 families, although there were frequent staphylococcal infections, no evidence of crossinfection could be obtained.

Rountree[228] reported that 35 to 40 per cent of soft-tissue infections seen by doctors in office practice in Australia were due to Type 80 strains of staphylococci. A later report on staphylococcal infections in general practice from the Australian National Health and Medical Research Council[280] also bears out the prevalence of phage Type 80 strains, often with no history of recent hospital contact. Direct or indirect hospital contact favors the development of the carrier state or lesions due to "epidemic," usually penicillin-resistant strains of staphylococci.[281,282]

It has been pointed out[283] that there are at least two groups of people for whom contact with a "hospital" staphylococcus may be particularly threatening. The first group consists of infants up to about two years of age, who seem to be particularly susceptible to staphylococcal pneumonia. Morris[284] has described this disease, which was formerly rare, as one of the most common serious diseases of infancy.

The second group at increased risk comprises those who become infected with one of the influenza viruses. In a study in the Netherlands, Goslings et al.[285] showed that the presence of staphylococcal skin lesions among members of a family was a significant factor in determining the incidence of staphylococcal pneumonia after an outbreak of influenza. Families with skin lesions had an unusually high incidence of postinfluenzal staphylococcal pneumonia.

It is likely that carriers of hospital strains who disseminate organisms in the hospital disseminate at home as well. Goslings[180] has shown that in the Netherlands about 6 per cent of the families become carriers of resistant strains of staphylococci when exposed to newborn carriers of the same strains. It seems reasonable to assume, therefore, that such disseminators, although particularly dangerous in a hospital environment, are also significant sources of contamination in the home and in the community. This may apply to patients as well as personnel.

Wise[286] has called attention to the necessity for scrupulous household hygiene, personal cleanliness and judicious use of antibiotics in eliminating staphylococcal disease from families in which multiple infections continually occur.

There are other ways in which the impact of staphylococcal crossinfection is felt in the community, socioeconomic in nature rather than bacteriologic. These are far more difficult to assess and need only be mentioned. Extended hospitalization and its attendant expense, loss of work, disability and death inevitably result in loss to the community.

Control of the community problem lies no longer with a single hospital or group of hospitals but, as has been undertaken in several communities, in full integration and utilization of hospital and community health planning and facilities.

Summary and Conclusions

Recent developments in the laboratory and epidemiologic aspects of the problem of staphylococcal crossinfection in hospitals are discussed. It would be well at this time to refer again to Figure 1, observing particularly where the several control measures directed against the organism itself, the person with a lesion, the carrier, air, contaminated objects in the environment and the susceptible host in the hospital all fit into the epidemiologic cycle of hospital crossinfection. This will also demonstrate the difficulty in assessing any one specific control measure since there are so many possible pathways of spread.

It becomes apparent that trends in investigation of the control of the problem are following two main avenues of approach:

Epidemiologic control. This approach is one that will gain momentum as more insight into the complexities of the source, reservoir and spread of staphylococcal infections is obtained. The limitation of this method of control is primarily the human factor, since so much depends on such practical points as: the reporting of lesions among hospital personnel and patients, the detection and management of the disseminating human carrier, the maintenance of all the environmental aspects of good housekeeping and ventilation of hospitals, as well as all the steps involved in good aseptic technics and isolation procedures, and the necessity of constant vigilance and continuing education of personnel.

Immunobiologic control. As more understanding of the basic biology of the organism and the immune mechanisms operating in the host is gained, any one of several immunobiologic approaches may eventually be found to circumvent the virulence or the antibiotic resistance of the staphylococcus or to increase the host's defenses. Trends in several such directions in present-day research are discussed in this review, and offer the hope of eventual success.

Interested readers may also wish to consult a recent British monograph[287] on this subject.

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Correction: In the Medical Progress report, "Staphylococcal Infection in Hospitals," by Drs. Nahmias and Eickhoff, which appeared in the July 13 issue of the *Journal,* the first sentence of the next to last paragraph in the left-hand column on page 78 should read as follows: "Staphylococci have been found to produce many factors: toxins — leukocidin, dermonecrotoxin, lethal toxin, erythrogenic factor, enterotoxin and hemolysins (alpha, beta, gamma, delta and epsilon); and enzymes — free and bound coagulase, fibrinolysin, hyaluronidase, phosphatase, protease, lipase, desoxyribonuclease and penicillinase."