MEDICAL PRACTICE

Hospital Topics

Isolating patients in hospital to control infection***Part I—Sources and routes of infection**

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The virtual disappearance of many infectious diseases has not removed the need to isolate patients. Sporadic cases and occasional outbreaks of the classical infectious diseases still occur. Moreover, the need for isolation has been recognised for other types of patients, such as those suffering from viral hepatitis and various hospital-acquired infections and for those who need protection while their defences against infection are impaired by disease or by treatment with cytotoxic or immuno-suppressive drugs.

In many older hospitals patients who need isolating have to be nursed in parts of a general ward unit set aside for that purpose. In newer hospitals isolation units are being built to replace the specialist infectious diseases hospitals. Both these arrangements introduce—in different degrees—the problems of caring for infective and susceptible patients in the same physical and nursing environment. In any part of a hospital the bacteriological factors that determine success or failure of isolation are in a constant state of flux, which makes the practice of isolation and its evaluation very difficult.

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Precautions against infection are often costly in money and the time of skilled staff and may be exasperating impediments to medical and surgical work. These are no excuses for neglecting essential precautions but they are good reasons why every precaution should be directed against a known hazard rather than against a merely theoretical risk. Unfortunately, this ideal requirement cannot be wholly fulfilled. Some of the sources and routes of infection in hospital have been clearly defined so that precautions against them are thought to be valid; but the relative importance of many is uncertain, because they have been insufficiently studied or because evaluation has proved too difficult. Precautions against infection have, in another context,¹ been classified thus: (a) those for which there is adequate bacteriological or clinical evidence of value, or both—*established methods*; (b) those that need more evaluation but can be regarded as *provisionally recommended methods*; (c) those that seem desirable but cannot be evaluated—*rational methods*; and (d) those that are traditionally observed but are probably unnecessary and may be harmful—*rituals*.

Much thought is now being given to the problems of designing and managing isolation units. It therefore seems timely to review present methods and to examine whatever evidence is available on their efficacy.

Sources and routes of infection

For most of the infections against which isolation in hospital is directed, human or animal bodies are the only sources in which human pathogens multiply and from which they start on their journey to another victim. The sources from which a susceptible tissue may become infected in hospital are therefore: (a) another site in the patient's own body—self infection; or (b) other patients, hospital staff, visitors, or food—cross infection.

From these sources organisms spread along the routes of

contact, fomite, and airborne infection. At various points they may accumulate to form reservoirs, from which secondary spread may occur. Very few pathogens can multiply in the inanimate environment, which is therefore more often a reservoir than a source.

Much of the epidemiological and experimental evidence of the importance of these sources, routes, and reservoirs depends on observations made not in isolation units but under normal ward conditions. This does not make it irrelevant, because isolation methods have to be devised to protect against the hazards of normal practices. The results of these researches should be borne in mind when the precautions, described in later parts of this paper, are being considered; some of them are clearly more relevant to source isolation and others to protective isolation.

Sources

SELF-INFECTION

The normal microbial flora of the human body consists largely of the organisms in the alimentary tract, upper respiratory tract, female genital tract, and the skin. This flora may include versatile pathogens, such as *Staphylococcus aureus*, that can cause disease in almost any tissue; others, such as *Micrococcus* species and diphtheroids, that are usually of very low pathogenicity; and many organisms with capabilities between these extremes.

Highly susceptible patients

The usual criteria of microbial pathogenicity do not apply for highly susceptible patients. For example, *Staph albus* (*epidermidis*), *Pseudomonas* species, and various fungi of usually low pathogenicity are opportunist invaders of patients whose defences against infection are impaired. These patients are therefore at continuous risk of infection by the normal flora of their own body.²⁻⁴ Infections from these sources show the limitations of protective isolation and have stimulated efforts to remove or reduce the endogenous microbial flora of highly susceptible patients.

Infected patients

Infected patients may also be at increased risk from their own organisms. The fact that aerial dissemination occurs from patients with septic dermatitis is well documented^{5, 6}; self-infection—for example, pneumonia arising from such a source during isolation⁷—may occur. Attempts to isolate these sources and others, such as boils, from other susceptible tissues in the same patient may sometimes be rational.

CROSS-INFECTION

Cross-infections may originate from patients or staff who are suffering from the relevant disease (cases) or who are symptomless carriers.

Cross-infection from cases

The risk from infected patients is well established. Many hospital outbreaks have been caused by the absence of good isolation facilities or failure to use them for patients who were sources of *Salmonella*, *Shigella*, *Pseudomonas*, enteropathogenic *Escherichia coli*, *Staph aureus*, *Streptococcus pyogenes*, or viruses. When these patients are free to move around a ward they may infect other patients directly. Even when isolated they may

infect other patients via the staff, who serve as mechanical vectors or may be infected and thus become new sources.

Hospital staff with infective disease have often been recorded as important sources of infection. Nurses and other staff with diarrhoea may infect patients and each other by direct or indirect contact: the frequent contamination of hands by intestinal pathogens is shown by the ease with which common intestinal organisms can be cultured from the unwashed hands of almost any person after defecation. Hutchinson⁸ isolated *Shigella sonnei* from lavatory seats and doorknobs after they had been used by people suffering from diarrhoea. Some strains of *Staph aureus*—for example, phage type 80/81—are especially likely to cause skin lesions in nurses, which may play a part in the rapid spread of *Staph aureus* infections through hospitals. There is at least one recorded instance of serious infections (one fatal) occurring after a surgeon operated when suffering from a severe staphylococcal lesion of the finger and axillary boils⁹; there is a corresponding—even if lesser—risk of infection from similar sources in wards. Hospital staff with common respiratory tract diseases usually remain on duty if the symptoms are not severe. They may not do great harm to most patients but they represent an unacceptable hazard to highly susceptible patients in protective isolation.

Cross-infection from carriers

There is plenty of evidence that symptomless carriers among patients and staff are important sources of infection; and there is no shortage of such carriers. In Western Europe the approximate carriage rates among the general population for some of the common pathogens are: *Salmonella* 0.2%, *Pseudomonas* 25%, enteropathogenic *E coli* 1%, *Staph aureus* 20-40%, and *Str pyogenes* 5-20%.

For intestinal diseases, symptomless carriers are often observed to be less dangerous than those with diarrhoea; the explosive spread of *E coli* enteritis from infants with diarrhoea is contrasted by the observation of Mortimer (personal communication) that spread was very uncommon from symptomless excretors among mothers and infants. This difference between cases and symptomless excretors may be a reflection of the relative numbers of the pathogens excreted or of the pathogenic and epidemiological properties of the strain; but the difference may be less important for excretors who prepare food, in which a small inoculum of pathogens may multiply to form a disease-causing dose. Similarly, staphylococcal dermatitis is more likely than symptomless skin carriage to cause profuse dispersal.⁵

But carriers of *Staph aureus* present a particular problem: even if symptomless carriers are individually less harmful than those with lesions, they are certainly more numerous and, collectively, may be a more important source. This organism thrives and multiplies in the nose and on the skin.¹⁰ For long it was thought that the nose was the only true site of *Staph aureus* carriage and that the skin became only secondarily contaminated from it; but Hare and Thomas¹¹ established that *Staph aureus* carriage occurs in the perineal region, and it may occur on other parts of the skin. Nose carriage is more common than skin carriage, so nose carriage often occurs without skin carriage but the converse occurs only occasionally.⁶ Nose swabbing is therefore more reliable than skin swabbing for detecting carriers. Although the nose is the main site of carriage, the skin may be more important as a source of infection. Nasal carriers shed very few *Staph aureus* organisms during normal breathing and speech^{11, 12}; in contrast, although most skin carriers of *Staph aureus* shed few of the organisms into their environment, some are "dispersers," who shed vast numbers of contaminated particles into the air around them.^{11, 13} They are presumably more potent sources of airborne or contact infection than carriers who are non-dispersers. Profuse *Staph aureus* dispersal by healthy carriers occurs from about 10% of young men and 1% of young women.^{14, 15} The reason for this sex difference, which

seems to be less pronounced in older people and hospital patients in bed,¹⁶ is unknown. The dispersed staphylococci are attached mainly to fragments of skin scales.¹⁷ Shedding can occur directly from the skin and the organism passes through the clothes; it does not depend wholly on a reservoir of skin scales in clothing.¹⁵

Patients' visitors

Visitors may serve as sources or vectors of pathogenic organisms in the same ways as the staff but are less likely to do so. For patients whose defence mechanisms are not seriously impaired, visitors are usually less dangerous because (a) for most pathogens the general public has a lower carriage rate than hospital staff; (b) the organisms they carry are less often of epidemic and antibiotic-resistant strains; and (c) their contacts with the patients are usually less close, less frequent, and less widespread. But, for patients whose condition justifies bacteriological screening of hospital staff, visitors must be regarded as potentially important sources of infection. Quite clearly, a patient may sometimes be a source of infection to visitors.

Food

The intestinal microbial flora of patients often changes during a stay in hospital. The organisms of classical food poisoning may be acquired from the raw material of hospital food or from staff in the kitchen. Patients also acquire identifiable strains of other intestinal organisms from hospital food.¹⁸

Pharmaceutical products

There are two ways in which pharmaceutical products may cause infection in hospital. Firstly, products that should be sterile are occasionally not, particularly fluids for intravenous use¹⁹⁻²⁰ and eyedrops,²¹ which are more likely to become contaminated when they are dispensed from multidose containers. Secondly, products that need not usually be sterile are sometimes excessively contaminated and occasionally contain pathogens; among those that have been recognised are pancreatic extract,²² thyroid extract,²³ and carmine dye²⁴⁻²⁵ contaminated with *Salmonella*; and lotions, skin creams, liquid soaps, and oral medicaments containing various organisms, among which *Pseudomonas* species was prominent.²⁶⁻²⁷ The growth of contaminants in pharmaceutical products is favoured by not date stamping containers and by "topping up" instead of returning and sterilising empty containers.

Disinfectant solutions cannot be considered self-sterilising. Solutions of chlorhexidine, quaternary-ammonium compounds, hexachlorophane creams, and even phenolics may contain high concentrations of pseudomonads and other Gram-negative organisms, particularly when their containers have been "topped up."²⁸⁻³⁰

Routes and reservoirs

PERSONAL CONTACT

Staff who are carriers of pathogenic organisms are sources who may transfer their organisms to patients and to their colleagues by contact of hands or of clothes. Staff who are neither symptomatic nor symptomless excretors of pathogens may serve as mechanical vectors, who convey microbes from one patient to another on skin or clothes. Lowbury *et al*³¹ found *Pseudomonas* species and Casewell and Phillips³² found *Klebsiella* species on the hands of ward staff; Speers *et al*³³ related contamination of nurses' uniforms to identifiable patient sources. Cleaning the

skin by washing is limited in respect of sites as well as frequency; and most clothing is permeable to skin scales and other small particles carrying infective agents, so that contamination is not confined to or by the outer garment. When the nurse attends another patient infective material may be transferred to his skin, clothing, bedding, or possessions. Wolinsky *et al*³⁴ have provided evidence that for staphylococcal infection of infants manual transfer is more important than the airborne route, at least when hand hygiene is poor. For other organisms in other situations, precise information of this sort is very scarce but there is some evidence that contact from hands and clothes is probably the main route by which organisms move from one patient to another in general hospital wards and isolation units.³⁵

Both staff who work mainly in one ward or department and those who work in many parts of a hospital may act as mechanical vectors.

BEDDING

Bedding becomes heavily contaminated with the microbial flora of the patients using it and, during bedmaking, contributes to contamination of the air. If bedding is not disinfected after use by each patient it may infect the next occupant, but there is little evidence that this happens very often. Bedding laundered at temperatures above 70°C is usually free from appreciable numbers of pathogens and remains so during storage in plastic bags; it is thus suitable for use by most patients but may not be so for highly susceptible patients in the extreme forms of protective isolation. Bedding can be contaminated during open storage and during bedmaking; Lidwell *et al*³⁶ found nurse-derived *Staph aureus* in about 75% of newly made beds.

EQUIPMENT AND FLOWERS

The many items of equipment that are known to become contaminated by patients include x-ray cassettes, stethoscopes,³⁷ sphygmomanometers,³⁸ baths and bowls,³⁹ shaving-brushes,⁴⁰ crockery, bedpans, urinals, and various types of respiratory apparatus. All these, as well as the many articles, including toys, that are traditionally referred to as fomites, are probably important occasionally or in special circumstances, but only respiratory apparatus⁴¹ and baths have been established as consistent reservoirs from which infection spreads easily and widely.

The water in flower vases usually contains a range of Gram-negative organisms including *Escherichia*, *Klebsiella*, *Pseudomonas*, and *Serratia*.⁴² The importance of this as a source of infection is uncertain.⁴³

STRUCTURAL ENVIRONMENT

Surfaces of walls, floors, and furniture become generally contaminated during normal use. Most of the organisms, even on floors, are of no medical significance. Although small numbers of *Clostridium* species are constantly present, human clostridial infections are usually derived from autogenous sources rather than from the environment. When a room is occupied by a patient who sheds pathogenic microbes, these can be recovered fairly easily from surfaces. Non-spore-forming pathogens, however, survive only a short time on walls and floors. *Staph aureus* survives, under natural conditions, only two to seven days⁴⁴⁻⁴⁵; Gram-negative organisms survive environmental drying less well than the Gram-positive cocci⁴⁶ unless they are embedded in protective material such as burn crusts.⁴⁷

There is evidence that streptococci⁴⁸ and staphylococci⁴⁹ that have survived environmental drying are reduced in virulence, but Laurell and Toth-Gyulase⁵⁰ were unable to confirm this.

Organisms contaminating walls and floors are not spontaneously released into the air⁵¹; dry-dusting and sweeping certainly disperse them, however, as does the use of inadequately filtered vacuum cleaners.⁵² Wet mops and buckets of cleaning fluid can be reservoirs from which floors become contaminated rather than cleaned.⁵³

The drain-traps of sinks often harbour pseudomonads.⁵⁴ Observations in one intensive care unit suggested that human infection rarely, if ever, occurred from this source⁵¹; but studies in another unit⁵⁵ suggested that infection could and sometimes did occur by back-splashing and contamination of the hands of staff.

Despite strongly held views on both sides, it remains uncertain whether the structural environment is important as a reservoir from which patients become infected or is merely a passive indicator of the presence of a source. Ayliffe *et al*⁵⁶ suggest that, although the risk of infection is high from equipment that comes into close contact with broken skin or mucosa or is introduced into body cavities, only intermediate or occasional risks are associated with medical and patient-care equipment that comes into close contact only with intact skin or mucosa of patients or the hands or clothes of medical, paramedical, and nursing staff. Low risks are associated with structural surfaces and domestic equipment.

THE AIR

Outdoor air usually contains fewer microbes than the air of occupied buildings and contains only infinitesimal numbers of human pathogens other than clostridia. In hospital, however, the air is being constantly contaminated with pathogens from the sources already discussed. Airborne particles shed by a patient or a member of the staff who is a profuse disperser may be carried by air that finds its way into another room by turbulent exchange or mass movement. Turbulence is caused by human movement or by thermal differences. In particular, opening or shutting a door causes considerable turbulence, which exchanges about 1 m³ (11 ft³) of air between the two sides of the doorway. Nursing patients in single rooms necessitates frequent entry into the rooms—about five to 10 times an hour.⁵⁷ Infective material may also be dispersed by a nurse who has contaminated her clothing when dealing with a patient. This dispersal may occur in the corridor, thus breaching the first of the two barriers to inter-room transfer of airborne material, or it may occur after the nurse has entered the room of another patient, thereby producing apparently airborne inter-room transfer, which may greatly exceed that which could arise from the movement of the air itself. Mass movement of air is caused by pressure differences due to natural or mechanical ventilation or to temperature effects, particularly in stairways.

The role of airborne infection in open wards has been studied mainly in relation to staphylococcal infections. Attempts have been made to relate the number of airborne *Staph aureus* to the prevalence of septic lesions and to the nasal acquisition of *Staph aureus* by patients and staff. Thus Noble⁵⁸ found that "broadcasts" of *Staph aureus* on 177 out of 732 ward days corresponded with increased nasal acquisition and once with an outbreak of sepsis. Lidwell *et al*⁶⁰ recorded higher than usual nasal acquisition of strains that had a great propensity for aerial spread. The role of airborne infection by staphylococci is indicated by records of reduced nasal acquisition and wound sepsis for patients who were nursed in single-bed rooms where the numbers of airborne staphylococci were reduced by controlled ventilation.⁶⁰⁻⁶² The general conclusion is that airborne staphylococci make a significant if variable contribution to infections perhaps directly but more often indirectly by causing nasal and skin colonisation of patients and staff. Comparable studies for other organisms are scarce but suggest that airborne infection is much less important for Gram-negative organisms.³

Flushing water-closet pans causes fairly substantial air contamination with any organisms that happen to be in the pan.⁶³

The contamination from wash-down pans was found to be 14 times that from siphonic pans; such an increase could cause appreciable contamination of surfaces with *Salmonella* or *Shigella* species after an excretor of one of these had used the pan.⁶⁴

Relative importance of various sources and routes

It is not easy to generalise on the relative importance of the various sources and routes and is dangerous to do so on the evidence from one epidemiological study. Nevertheless, for *Staph aureus* it seems that self-infection and cross-infection are both important.⁶⁵⁻⁶⁶ For the cross-infections nasal carriers and septic lesions may be about equally important as sources.⁶⁰ In some studies patients acquired infections with about equal frequency from other patients and from staff, but even more were acquired from untraceable sources.⁶⁷⁻⁶⁸ Airborne and contact infection are both important, though not necessarily in the same circumstances and at the same time. Infections with coliforms are often autogenous, arising from the faecal flora.³ Infections with *Clostridium* and *Candida* species are also usually autogenous. Pseudomonas infections, however, are only rarely autogenous, cross-infection being mainly by human contact and perhaps from food.

Perhaps the most important generalisation that can be made with any certainty is that the importance of sources of organisms and routes of spread is extremely variable, depending on the profusion of the source, the occupation of the source person, the precautions being applied at the time, and the existence of a susceptible tissue at the end of a route of spread at the time the organism reaches it. It is this variability that makes attempts at evaluation so difficult.

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Parts II-V of this paper will be published in future issues.

Today's Treatment

Use of antibiotics

Aminoglycosides*

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Indications for clinical use of aminoglycosides in hospital and hospital clinics

LIFE-THREATENING SEPSIS CAUSED BY COLIFORMS, PS AERUGINOSA, AND STAPH AUREUS

Gentamicin and the other systemic aminoglycosides (amikacin and tobramycin) are the first choice antibiotics in life-threatening sepsis caused by coliforms, *Ps aeruginosa*, and *Staph aureus*. Sepsis with coliforms (*E coli*, klebsiella, enterobacter, serratia, proteus, citrobacter), *Ps aeruginosa*, and *Staph aureus* is particularly common in hospital and is more likely to affect debilitated patients such as those undergoing major surgery, those with malignant disease or receiving cytotoxic, steroid, or irradiation treatment, or both, the elderly, neonates, those with indwelling catheters or intravenous lines, and those receiving assisted ventilation. It may present as septicaemia with or without shock, as pyelonephritis, pneumonia, severe wound infection, peritonitis, drip-site infection, hepatic abscess, or cholangitis. In these cases it is imperative to begin antibiotic treatment after specimens such as blood cultures, sputum, urine, wound swabs,

etc, have been taken, but before culture and sensitivity test results are available. Gentamicin (or other aminoglycoside) is chosen because of its wide spectrum of activity and its potent, rapid bactericidal action. When the infection is controlled and culture and sensitivity test results are available it may be reasonable to change treatment to some other suitable agent.

In certain cases (generally where mixed bacterial infection is suspected or where synergy is needed) other antimicrobial agents should be combined with gentamicin (or other aminoglycoside).

Anaerobes—Mixed infections including coliforms and anaerobes may be strongly suspected after gastrointestinal surgery or perforation, subphrenic abscess, empyema of the gall bladder, liver abscess, female genital tract sepsis or surgery, aspiration pneumonia, and empyema of the chest. A suitable antianaerobic agent should be combined with the aminoglycoside. The present choice is between metronidazole (my own current preference usually), clindamycin, chloramphenicol, or possibly high dosage erythromycin.

Streptococci—If streptococci are strongly suspected as in endocarditis, cellulitis, or pneumonia, or in patients with hepatocellular liver disease and septicaemia, then a penicillin (benzylpenicillin or ampicillin) should be added.

Staphylococci—When sepsis with *Staph aureus* is strongly suspected as in severe postoperative wound infection, postviral pneumonia, acute endocarditis, then flucloxacillin (or cloxacillin) should be added in high dosage. Although gentamicin (tobramycin) is effective alone against most strains of *Staph aureus*, the high dose of β -lactam antibiotic helps eradicate staphylococci from soft tissues etc.

Neutropenia—The major bacterial pathogens known to infect these patients include coliforms, *Ps aeruginosa*, and *Staph*

*The first part of Dr Noone's paper was published last week (p 549), together with the tables and references.