

PAPERS AND ORIGINALS

A unit for source and protective isolation in a general hospital

G A J AYLIFFER, J R BABB, LYNDA TAYLOR, R WISE

British Medical Journal, 1979, 2, 461-465

Summary and conclusions

An isolation unit consisting of 12 ventilated cubicles was investigated over 18 months. Out of 462 patients admitted, 262 (57%) required source and 200 (43%) protective isolation. Admissions of patients with staphylococcal sepsis fell from 16 in the first three months to six in the last three months. *Staphylococcus aureus* was recovered from 12% of nurses' fingers and often in small numbers from protective clothing and uniforms, but only two patients acquired a strain from a nurse or another patient. Gram-negative bacilli were rarely recovered from hands or protective clothing of nurses, and there was no evidence of spread of infectious diseases.

This inexpensive unit, with simple but efficient isolation-nursing techniques, successfully prevented the spread of infection.

Introduction

The spread of infection is prevented by effective surveillance, good hygiene techniques, rapid implementation of preventive measures, and isolating infected or susceptible patients. Although surveillance and good hygiene techniques are possible in any hospital, most older hospitals in the UK have inadequate isolation facilities.¹ Owing to the greater awareness of hazards of infection by the general public in the past few years hospital authorities will be expected to provide greater protection against hospital-acquired infection. Bagshawe *et al*² provided excellent advice on isolation techniques and units, but these are expensive to build, are time-consuming for staff, require a high staff-

patient ratio, and most general hospitals probably cannot afford separate units for source and protective isolation.

Since the isolation facilities at this hospital were mainly restricted to one or two side rooms attached to large open wards, it was decided to convert an existing ward into an isolation unit. Funds were limited, and it was not possible to construct self-contained cubicles with air-locks as described elsewhere.³ Nevertheless, plenum ventilation was provided for the cubicles. The ward was opened in January 1977.

The aims of the present study were (1) to study cross-infection and the spread of organisms in the unit; (2) to assess the value of the unit to the hospital and to investigate the problems of nursing infected and susceptible patients in the same unit; (3) to provide training for nursing and other staff and to study the techniques of isolation nursing; and (4) to determine the effect of the unit on staphylococcal cross-infection in the hospital and to provide intensive treatment for patients with severe or chronic localised sepsis.

Description of isolation ward

A ward containing two plenum-ventilated isolation units, two other ventilated rooms, and 14 beds in an open area⁴ was converted into a completely cubicalised ward. Twelve single-bedded cubicles, of which only the two original self-contained plenum-ventilated units remained, were sited on each side of a corridor. The new cubicles contained a wash-hand basin but no toilet, bath, shower, or air-lock. Bathing and toilet facilities were provided at one end of the unit. The ward itself was sited in the acute area of the hospital on the first floor and opened on to one of the main corridors. A plenum-ventilation system supplied filtered warm air (seven changes/hour) to the new cubicles, the two original cubicles retaining their system providing 20 air changes/hour. The new cubicles were also fitted with an extractor fan capable of removing air to the outside (at either 14 or 20 changes/hour). When cubicles were required for protective isolation the extractor fans were turned off. Thus air flows were from the cubicle to the central corridor for protective isolation, and from the corridor to the cubicle and thence to the outside via the extractor fan for source isolation.

Hospital Infection Research Laboratory and Microbiology Laboratory, Dudley Road Hospital, Birmingham B18 7QH

G A J AYLIFFE, MD, FRCPATH, consultant microbiologist

J R BABB, FIMLS, senior research officer

LYNDA TAYLOR, SRN, SCM, research sister

R WISE, MB, MRCPATH, consultant microbiologist

ADMISSIONS

Patients were admitted to the ward if they were particularly susceptible to infection—for example, patients with leukaemia and

those receiving immunosuppressive treatment—or if a communicable infection was diagnosed or suspected. Communicable infections included the following three categories.

Category 1 comprised (a) heavy or potential dispersers of staphylococci or patients infected with highly resistant strains of *Staphylococcus aureus*—for example, resistant to methicillin (cloxacillin), lincomycin, fusidic acid, or gentamicin—or receiving certain antibiotics to which resistance was likely to develop—for example, fusidic acid; (b) patients with severe sepsis caused by *Streptococcus pyogenes*; and (c) patients transferred from a skin hospital or suffering from overt skin disease, who were isolated in the unit until bacteriological sampling confirmed they were not carrying or dispersing undesirable strains of *Staph aureus*.

Category 2 comprised patients with suspected infectious diseases—for example, with diarrhoea and vomiting—before a diagnosis was made.

Category 3 comprised patients with diagnosed infectious diseases—for example, salmonella or shigella infections, active pulmonary tuberculosis, or childhood infectious fevers—who were admitted before transfer home or to the infectious diseases hospital. Occasionally these patients were retained for clinical reasons. Patients with hepatitis or salmonella infections other than *Salmonella typhi* were not usually transferred to the infectious diseases hospital.

Admissions and discharges were decided on the basis of infection hazard or susceptibility by an infection control officer (consultant microbiologist) in collaboration with the clinician concerned. Clinicians could admit patients without consultation, however, if isolation was clearly required and beds were available. Patients were referred from other wards, from other hospitals in the district, from the casualty department, and from the occupational health department.

WARD PRACTICE

Since infected and susceptible patients were treated in the same ward, scrupulous attention was given to hygiene. Hands of staff were washed in a chlorhexidine-detergent preparation (Hibiscrub) before attending a patient receiving protective isolation and before leaving the cubicle of a patient receiving source isolation. Cotton gowns or disposable plastic aprons were worn only when a patient or his immediate surroundings were handled and not routinely on entering a cubicle. The gowns and aprons were hung in the cubicle and changed daily. Masks were not worn and gloves only when contaminated material was handled.

Doors of cubicles were kept closed, particularly when another patient was in the corridor. During bedmaking and periods of similar high activity the extractor fans in cubicles of patients undergoing source isolation were turned to maximum (20 changes/hour). Immunosuppressed patients with low neutrophil counts ($< 1.0 \times 10^9/l$ ($< 1000/mm^3$)) were kept, if possible, in one of the two original cubicles, which contained a shower, toilet, and air-lock.

Visitors were not restricted, other than the ordinary maximum of two at a time, but wore gowns or aprons when in close contact with the patient. Children were restricted to some extent, depending on the infection or type of patient in the cubicle.

Special care was taken to ensure disinfection of the bath, shower, and toilet with a non-abrasive hypochlorite powder after use by an infected patient. Rooms were cleaned by specially trained domestic staff, and the order of cleaning was defined—that is, a cubicle containing a patient requiring protective isolation was cleaned first. A phenolic disinfectant was used for all cubicle cleaning apart from rooms of patients with hepatitis, where hypochlorites were used. Coloured cards indicated patients requiring source (blue) or protective isolation (white) and those with hepatitis (yellow). No other information was on the card except the name of the consultant in charge of the patient.

A labelled refrigerator was used to maintain stocks of culture plates, swabs, and specimens awaiting collection by laboratory staff. Specimens leaving the ward were enclosed in a polyethylene bag clearly labelled and secured. All laundry was treated as infected, and linen from patients with enteric infections, hepatitis, or open pulmonary tuberculosis was placed in a water-soluble bag. These were tied at the neck and placed in colour-coded nylon laundry bags. Crockery and cutlery were washed and disinfected by heat in a washing-up machine, and bedpans were disinfected in an automatic washer with a steam cycle.

STAFF HEALTH

Staff working in the ward received a pre-employment medical examination and were immunised as required—for example, with BCG if tuberculin-negative and oral poliomyelitis vaccine. Female staff were tested for rubella antibodies. Chest radiography was performed yearly. All staff were expected to report superficial sepsis to the ward sister, and to the occupational health department if suffering from any other infection.

Materials and methods

Patient sampling was carried out by either the nursing or laboratory staff. Nose swabs were taken from all patients twice weekly. Throat and vaginal swabs, midstream urine and stool specimens, and sputum if appropriate were taken from patients with leukaemia on admission. Wound swabs were taken on admission, weekly, or on removal of dressings.

Staff sampling—Nose swabs and random finger-streak samples were taken weekly from nursing staff. Contact plates were taken weekly from the fronts of gowns, plastic aprons, and nurses' uniforms at bed height. This is the area of maximum contamination.⁵

Air sampling—Several tests were made in cubicles before the ward was occupied. These included air-flow measurements and tests on the removal or escape of nebulised spores or natural contamination produced by vigorous exercise or bedmaking. Routine air sampling was made twice weekly with a slit-sampler in the corridor and cubicles of possible staphylococci dispersers. Two large settle plates (14 cm diameter) were also exposed twice weekly for four hours in the cubicles of patients requiring protective isolation.

Surveys in other wards—A cross-sectional survey had been made yearly in all wards of the hospital⁶ since 1968. Nose swabs and wound swabs were taken from patients, and nose swabs from all nurses on duty at the time of the survey.

Bacteriological methods—Nose swabs were cultured on nutrient agar plates containing 0.01% phenolphthalein diphosphate, 1% horse serum, and 10 mg tetracycline/l during the early part of the study. The same medium with and without tetracycline was used for contact finger-streak and air-sampling plates. Wound swabs were cultured aerobically and anaerobically on blood agar and on MacConkey's agar. Antibiotic sensitivity tests were made on phosphatase-producing strains of *Staph aureus* isolated from all sources. These strains were confirmed by coagulase or deoxyribonuclease tests, and most were phage-typed.

Results

ADMISSIONS

During the first 18 months of the study 462 patients were admitted to the ward, 262 (57%) for source isolation and 200 (43%) for pro-

TABLE 1—Distribution of patients admitted to ward for source isolation and protective isolation and durations of stay

	Source isolation		Total	Protective isolation		Total
	Hospital sepsis*	Communicable and enteric infections		Patients with leukaemia	Others immunologically compromised	
No (%) of patients	61 (13.2)	201 (43.5)	262 (56.7)	108 (23.4)	92 (19.9)	200 (43.3)
Mean duration of stay in days (range)	22.5 (1-99)	7.3 (1-151)			8 (1-86)	

*Includes 51 staphylococcal infections.

fective isolation (table I). Table II lists the diagnoses of patients admitted for source isolation. On average seven of the 12 beds were occupied during the period. Patients with staphylococcal infections remained in the ward considerably longer than those requiring protective isolation. Fig 1 shows the change in distribution of admissions over the 18 months. In the first three months 16 patients were admitted with staphylococcal sepsis compared with only six in the last three months. The number of immunosuppressed patients increased over the same period, but many of these were admitted for a few days only for a course of treatment. Admissions of patients with diagnosed or suspected infectious disease remained relatively constant apart from a period when several non-immune contacts of chickenpox were admitted during an outbreak in the children's wards (July-September 1977). Children with infections, if not sent home or transferred to the infectious diseases hospital, usually remained in side wards in the paediatric block.

TABLE II—Diagnoses of 262 patients admitted to ward for source isolation

Admission group and diagnosis	No of patients
Staphylococcal infections:	
Varicose ulcers and pressure sores	15
Surgical wounds	16
Dispersers/carriers	6
Requiring special antibiotics	14
Other sepsis:	
Septicaemia, β -haemolytic streptococcal infection, etc	10
Enteric infections:	
Non-specific diarrhoea and vomiting	41
Salmonella infections or carriers (22), shigella infections (4), etc	28
Tuberculosis:	
Confirmed	33
Suspected	28
Viral hepatitis:	
Confirmed	9
Suspected	17
Childhood fevers:	
Rubella, measles, mumps, chickenpox	17
Non-immune contacts	13
Other infections:	
Meningitis, malaria, pyrexia of unknown origin, etc	15

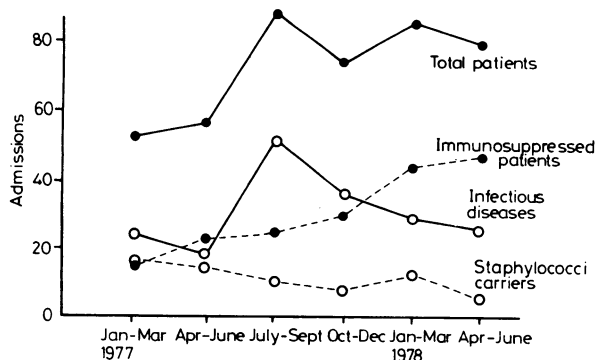


FIG 1—Change in distribution of admissions during study period.

INFECTION IN PATIENTS

Only one patient acquired a strain of multiple-resistant *Staph aureus* from another patient. His nose was colonised after emergency packing for haemorrhage, and the organism was probably transferred on the hands of the attendant. One patient with leukaemia developed septicaemia with a penicillin-resistant strain of *Staph aureus* of a similar phage-type carried by a nurse. Several leukaemic and immunosuppressed patients developed an infection either in the ward or before admission, but from the strains isolated these appeared to be endogenous in origin. There was no evidence of cross-infection with infectious diseases.

STAPHYLOCOCCAL CROSS-INFECTION IN THE HOSPITAL

The yearly cross-sectional surveys showed a reduction in tetracycline-resistant staphylococci in the noses of patients and nurses since 1968 (fig 2). The wounds of patients showed a similar reduction, but numbers in the surveys were too small for adequate assessment.

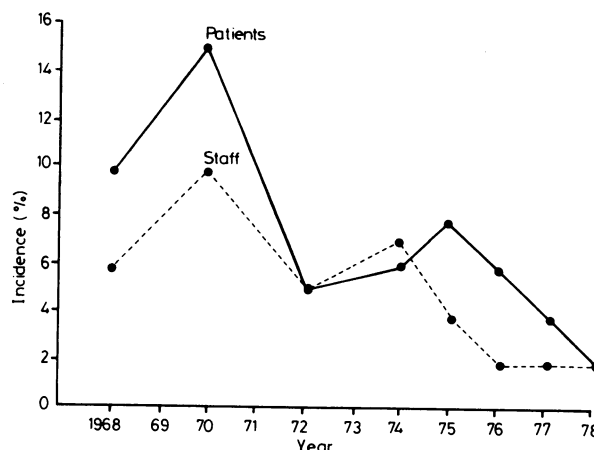


FIG 2—Incidence of nasal carriage of tetracycline-resistant *Staph aureus* in patients and staff of hospital during 1968-78.

The reduction appeared to be greater during 1977 and 1978 after opening the isolation ward.

SAMPLING OF STAFF

Noses—Out of 658 nose swabs examined, only eight from three members of staff grew tetracycline-resistant or multi-resistant strains of *Staph aureus*. Only one member persistently carried a resistant strain, which was not acquired in the ward. None of the multi-resistant strains were transferred to patients.

Hands—Of the 605 finger-streaks examined, 74 (12.2%) yielded *Staph aureus* (table III), of which 20 (27%) were multi-resistant. All the resistant strains were directly related to patients nursed in the ward at the time. The association of sensitive strains with patients was more difficult, but patient-associated strains were common. Gram-negative bacilli were isolated from only five of the plates (0.8%). Isolates of *Staph aureus* and in particular Gram-negative bacilli from fingers were fewer than in other wards.

TABLE III—Recovery of *Staph aureus* and Gram-negative bacilli from nurses' hands

	No of hands sampled	No (%) of finger-streak plates yielding:	
		<i>Staph aureus</i>	Gram-negative bacilli
Isolation unit	605	74 (12.2)	5 (0.8)
Other wards	112	27 (24.1)	19 (17.0)

PROTECTIVE CLOTHING AND NURSES' UNIFORMS

Staph aureus was often isolated in small numbers from clothing, but Gram-negative bacilli were surprisingly rare (table IV). By means of antibiograms and phage-typing, 25 of the 26 isolations of

TABLE IV—Recovery of *Staph aureus* and Gram-negative bacilli from clothing of staff

	No of colony-forming units/25 cm ²	Cotton gowns (n = 207)	Plastic aprons (n = 239)	Uniform dresses (n = 588)
<i>Staph aureus</i>				
1-5	20	17	77	
6-10	1	3	7	
>10	5	2	5	
Total	26 (12.6%)	22 (9.2%)	89 (15.1%)	
Gram-negative bacilli				
1-5	1	0	7	
6-10	0	0	5	
>10	0	0	1	
Total	1 (0.5%)	0	13 (2.2%)	

Staph aureus from cotton gowns and 21 of the 22 from plastic aprons could be associated with the patient in the cubicle at the time of sampling. Of the 89 isolations from nurses' uniforms 31 (35%) were associated with patients, but 42 (47%) could not be associated with any source; 16 (18%) were the nurses' own strains.

AIR SAMPLING

Preliminary tests in unoccupied cubicles showed that airborne contamination was rapidly removed during conditions of both source isolation and protective isolation. Of spores released in a cubicle during source isolation, none were isolated in the corridor when the door remained closed. A few spores (fewer than 1%) were isolated in plenum cubicles when 100×10^6 spores were released in the corridor immediately outside a closed door. In routine sampling of the corridor, 67 (11.2%) out of 600 samples, each of 50 cu ft (1.4 m³), contained tetracycline-resistant *Staph aureus*. Of plates growing resistant strains, 88% yielded counts of less than 5 and under 1% yielded more than 10 colonies in 1.4 m³ of air. These were often associated with a patient in the corridor or an open door. *Staph aureus* was isolated from 9.2% of plates exposed in protective cubicles. On only two occasions were strains found that were similar to those from other patients in the ward, and these were present in small numbers—that is, 1 or 2 colonies. On one occasion a patient in protective isolation was found to be a staphylococci disperser, 47 colony-forming units being counted on one settle-plate.

Discussion

This system for isolating both infected and susceptible patients in the same unit was found to be effective. Even when a heavy staphylococci disperser was present in the ward the strain was rarely found in other cubicles, and there was little evidence of cross-infection during two and a half years. The system in the ward was simple and inexpensive. The initial structural costs could probably be further reduced without increasing the risk of spread of infection. The possible deficiencies—namely, the central corridor and absence of individual showers, toilets, and air-locks (apart from in the two self-contained units)—did not appear to detract from the effectiveness of the ward. Success depended on the nursing staff ensuring that doors were kept closed and that toilets, baths, and showers were disinfected after use by infected patients. The most important measure was handwashing before carrying out a procedure on a susceptible patient and after a procedure on an infected patient. Protective clothing was kept to a minimum; masks and gloves were rarely worn, and overshoes and protective caps or hats were not used. Visiting was not restricted. Sampling of staff, noses, hands, air, and clothing was carried out as a research procedure but is not considered necessary as a routine unless there is evidence of spread of infection.

The effect of the ward on cross-infection in the hospital is difficult to assess since there has been a reduction in staphylococcal cross-infection over the past 10 years. This is part of the general trend occurring in many hospitals.⁷ The pronounced decrease in the past two years, however, may have been partly due to the presence of the isolation ward. Highly resistant strains—that is, resistant to methicillin, lincomycin, and fusidic acid—still occasionally appear, and an important function of the isolation ward is to ensure the elimination of these strains from the hospital as well as to prevent spread. Patients carrying these strains often have chronic infections, such as bedsores and varicose ulcers, and the ward is particularly suitable for intensive local treatment. Other advantages include nursing patients with enteric fever when transfer to the infectious diseases hospital is undesirable for clinical reasons. The isolation of non-immune, long-stay children who are contacts of communicable diseases reduces the necessity of closing other wards. Although hepatitis is not readily transmissible, nursing by skilled staff reduces the risks of accidents. Cross-infection with *Klebsiella* sp has occurred in the hospital as in many others in the UK,⁸ but patients with Gram-negative surgical or urological

infections were not usually isolated in the ward. Nevertheless, if strains resistant to gentamicin or recently developed antibiotics were detected, patients carrying these strains would be isolated in the ward.

Staph aureus was chosen as the most suitable organism to measure cross-infection. It survives better than Gram-negative bacilli in the "dry" environment, it is the only potentially pathogenic organism that spreads in the air and can be easily typed, and a patient carrying a known phage type was usually present in the ward. Faeces were not routinely examined for the acquisition of enteric pathogens, but there was no evidence of clinical transfer. Environmental sampling in rooms or sites used by patients with enteric fever showed no salmonellae apart from an occasional colony on the toilet or shower seat before cleaning. The possible transfer of other Gram-negative bacilli will be investigated in a later study.

When the ward was originally planned, seven or eight years ago, it was calculated that two-thirds of the patients would be isolated for hospital sepsis. At present the ward is mainly occupied by patients requiring immunosuppression. Although infections (or suspected infections) in such patients are not uncommon, they appear to be mainly endogenous, and the patients are often admitted with infection from home. The minimal precautions against cross-infection appear to be effective in protecting these patients, and they are not disturbed by excessive restrictions. Treatment of all patients, infected and susceptible, in one unit ensures the best care by trained staff. The main problem could be the possible transfer of highly infectious diseases, such as chickenpox, to immunosuppressed patients. Whenever possible such infected patients are sent home or to the infectious diseases hospital, but the main risk is the possible transfer of infection from a member of staff who is incubating the disease. Reliable laboratory tests for measuring immunity in staff would be useful, although whenever possible non-immune nursing staff do not nurse infected patients.

Barrier-nursing is tedious and rarely done properly in general wards and requires additional nursing staff. The use of different staff for nursing susceptible and infected patients is generally advisable but does not appear to be necessary if the staff are well trained and precautions are kept to a safe minimum. Although no obvious difference in protective effect was shown between the cotton gowns and plastic aprons, the apron is cheap, impermeable to moisture and bacteria, comfortable, and should be more effective.⁹ Nevertheless, a gown provides better protection when lifting patients and is preferred by nurses for some procedures. Gowns of less permeable materials than cotton may be more suitable.¹⁰ Contamination of nurses' uniforms with *Staph aureus* is undesirable and, although isolates of staphylococci in the air of protective cubicles were minimal, further studies on clothing are needed to minimise these risks. The infrequent isolation of Gram-negative bacilli suggests that clothing is not an important mode of transfer. Counts of potential pathogens on fingers were generally lower than in other wards. From laboratory studies this was probably due more to diligent handwashing than to the use of an antiseptic preparation, and further studies using non-medicated soap are in progress.^{11,12} The inanimate environment of a cubicle is of minor importance in the transfer of infection. Although disinfectants are used on floors and furnishings, cleaning should be adequate and disinfectants are used mainly to allay fears of infection in the domestic staff. Terminal disinfection does not entail cleaning walls and ceilings or changing curtains.

The main problems in the ward were similar to those in other special units, such as intensive care. The number and types of patients are variable and nursing care is often intensive. The staff sometimes have too much work, while at other times there is too little. A nursing staff of 19 appeared to be adequate on most occasions, but this number was not always attainable. Internal rotation of staff to include night duty is necessary to maintain standards throughout the day and night.

Psychological problems of isolation in adults and children are kept to a minimum by constant attention by the nursing staff, allowing almost unrestricted visiting, and supplying each patient with a television set. A further problem concerned the transfer of chronic salmonellae carriers to geriatric units; in one instance a carrier remained in the ward for six months. Nevertheless, the selection of patients and decisions on discharge are not usually a problem, and the infection control officers make the final decision in the event of disagreement.

An isolation unit fulfils a useful role in a general hospital despite the cost of nursing staff. The number of cubicles (12 for a hospital of 730 patients) was generally adequate, and a smaller unit would not be viable. More cubicles—say, up to 20—might be required if children with infections were also routinely nursed in the ward. More patients, however, may create additional nursing problems, including a range of specialist knowledge and experience, and standards may fall. It should be possible to keep all patients with communicable diseases in such a unit—apart from long-term patients with, say, tuberculosis—but this also depends on the isolation requirements for immunosuppressed patients. It would rarely be justified, owing to expense and other problems of special units, to have separate wards for infected and immunosuppressed patients. The cost of the unit itself could be reduced by lessening the complexity of the ventilation system without greatly increasing the risk of infection. Providing extractor fans in four cubicles would probably be enough to reduce the risk of

airborne spread from the more highly communicable diseases, but supplementary heating may be required, as heat loss may be excessive. Preventing contact spread is much more important than preventing airborne spread, and simple and safe techniques are all that are required provided that the very highly communicable or dangerous infections—for example, Lassa fever—are excluded.

We thank Sister A Etheridge and the nursing staff of the ward for their co-operation, and Mrs J Davies and Miss C Bradley for technical help.

References

- 1 Ayliffe, G A J, *et al*, *Lancet*, 1969, **2**, 1117.
- 2 Bagshawe, K D, Blowers, R, and Lidwell, O M, *British Medical Journal*, 1978, **2**, (in five parts) 609, 684, 744, 808, 879.
- 3 Tyrell, D A J, *et al*, *British Medical Journal*, 1977, **2**, 373.
- 4 Ayliffe, G A J, *et al*, *Journal of Hygiene*, 1971, **69**, 511.
- 5 Speers, R, *et al*, *Lancet*, 1969, **2**, 233.
- 6 Ayliffe, G A J, *et al*, *Journal of Hygiene*, 1977, **79**, 299.
- 7 Ayliffe, G A J, Lilly, H A, and Lowbury, E J L, *Lancet*, 1979, **1**, 538.
- 8 Caswell, M, and Phillips, I, *British Medical Journal*, 1977, **2**, 1315.
- 9 Lidwell, O M, *et al*, *Journal of Applied Bacteriology*, 1974, **37**, 649.
- 10 Hambraeus, A, *Journal of Hygiene*, 1973, **71**, 799.
- 11 Ayliffe, G A J, Babb, J R, and Quorairshi, A H, *Journal of Clinical Pathology*, 1978, **31**, 923.
- 12 Taylor, L J, *Nursing Times*, 1978, Jan 12, p 54, Jan 19, p 108.

(Accepted 9 July 1979)

Effects of inflammatory disease on plasma oxprenolol concentrations

M J KENDALL, CHARMAINE P QUARTERMAN, HILARY BISHOP, R E SCHNEIDER

British Medical Journal, 1979, **2**, 465-468

Summary and conclusions

When single oral doses of oxprenolol were given to three healthy subjects on three separate occasions under standardised conditions the plasma concentration-time curves for each subject were closely similar. In two of the subjects, however, a mild illness led to a dramatic, temporary increase in the peak plasma concentration and area under the plasma concentration-time curve (AUC). This effect of inflammatory disease was confirmed by comparing a group of patients with an erythrocyte sedimentation rate (ESR) of over 20 mm in the first hour with a group whose ESR was below this value. The mean peak plasma concentration and AUC were significantly higher in the group with a raised ESR. This may be related to altered concentrations of one of the acute-phase proteins.

Thus it is concluded that plasma oxprenolol concentra-

tions are raised in inflammatory disease, but further work is needed to determine the mechanism of this increase.

Introduction

Drugs are usually given to young, healthy volunteers before being given to patients. Care must then be taken when extrapolating from data on blood concentrations obtained in this way to patients, who are often older, may be taking other drugs, and are ill. Patients with various inflammatory diseases attain much higher plasma propranolol concentrations than healthy controls.¹ This prompted us to assess the effects of inflammatory disease on the plasma concentrations of other beta-blockers differing from propranolol in their protein-binding characteristics and route of elimination. Oxprenolol is less protein bound (70% as opposed to 93%²), and most is conjugated with glucuronic acid by the liver, unlike propranolol, which is degraded to several metabolites.³

We report here the results of two separate studies. The first determined the reproducibility of the plasma concentration-time curves of oxprenolol in three subjects. In two of these the fortuitous development of an acute infection during the study allowed us to assess the effect of such an illness on the plasma oxprenolol concentrations. In the second study we compared the plasma oxprenolol concentrations in a group of patients with chronic inflammatory diseases associated with a raised erythrocyte sedimentation rate (ESR) with those in a group of subjects with normal ESR values.

Department of Therapeutics and Clinical Pharmacology, Queen Elizabeth Hospital, Birmingham B15 2TH

M J KENDALL, MD, MRCP, senior lecturer in therapeutics and clinical pharmacology, and honorary consultant physician
CHARMAINE P QUARTERMAN, BSc, research technician
HILARY BISHOP, research technician
R E SCHNEIDER, MD, FRCPED, senior honorary research fellow