bacteria were isolated might also have yielded anaerobes had transport and laboratory conditions been optimal.

Wide surgical drainage is the established treatment for axillary abscesses, and its efficacy was clearly shown in this series as only three abscesses, caused by *Staph aureus*, recurred. Hidradenitis suppurativa presents a quite different clinical picture of multiple small abscesses with undermining and induration of the axillary skin and persistent foul discharge. Three of our seven patients underwent surgical drainage in the acute phase and were treated with metronidazole for two or three weeks. In two patients the infection did not recur, and the third was lost to follow-up. The patient in case 8 attended the casualty department almost weekly for 10 months with recurrent bilateral anaerobic abscesses after the birth of her second child. Three abscesses required repeated drainage, and she received metronidazole for six weeks with minimal effect and unacceptable nausea. She was finally cured by wide excision of the axillary skin. The patient in case 12 responded partially to metronidazole, the discharge lessening and its foul odour disappearing. Surgery was planned but not until drastic weight loss had been achieved. Two further patients underwent surgery with satisfactory results.

Hidradenitis suppurativa is traditionally believed to be a disease of apocrine sweat glands, although the keratin plugging that characterises this condition⁹ affects the pilosebaceous follicles rather than sweat ducts. In our cases the histological appearances suggested apocrine and pilosebaceous obstruction, and both may be important in promoting infection. We have recently emphasised the association of keratin plugging of

breast ducts with anaerobic infection in non-puerperal subareolar breast abscesses.⁴

Axillary abscesses are one of the commonest cutaneous infections and when associated with foul pus can be assumed to be anaerobic. Whether antimicrobial agents have an important role in managing most abscesses of this type, whatever the pathogen, is doubtful. Recurrent axillary sepsis and particularly hidradenitis suppurativa seem to suggest secondary infection with anaerobic bacteria of an underlying structural abnormality. While antimicrobials with specific activity against anaerobic bacteria may help in controlling acute exacerbations of hidradenitis suppurativa and certainly reduce the putrid odour of the discharge, patients with this condition usually require extensive surgical intervention to effect a permanent cure.

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Hospital outbreak of trimethoprim resistance in pathogenic coliform bacteria

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Summary and conclusions

In an investigation of outbreak of infection caused by coliform bacilli with plasmid-mediated trimethoprim (TMP) resistance many patients were found to be asymptomatic carriers of TMP-resistant coliform bacilli. Analysis of factors predisposing to rectal carriage of these organisms showed that the most important was previous treatment with co-trimoxazole, a sulphonamide, or ampicillin. The outbreak was controlled by a policy restricting the antibiotics given.

Geriatric units are an important source of hospital infection. When an outbreak occurs the logical sequence of steps to be taken is to monitor cases, identify the outbreaks, analyse the causative factors, plan corrective action jointly with laboratory staff, and monitor the outcome.

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Introduction

Co-trimoxazole, a combination of sulphamethoxazole and trimethoprim (TMP), was released for clinical use in 1969. Although strains of coliform bacteria resistant to TMP were found before the drug was introduced,¹⁻³ bacterial resistance to TMP has not generally increased.⁴ Initially, resistance to TMP was thought to be chromosomal, but in 1971 it was shown⁵ that some patients in St Pancras Hospital had infections due to coliform bacilli carrying R factors mediating TMP resistance. We describe an outbreak of plasmid-mediated TMP resistance in coliform bacilli isolated from patients in that hospital between 1972 and 1976 and the methods used to control it.

Methods

Identification of infection due to TMP-resistant bacilli—Specimens were cultured by standard techniques, and antimicrobial sensitivity tests were performed by Stokes's technique⁶ using discs containing 1.25 mg of TMP. Such tests were performed on organisms thought to be causing infections that might reasonably be treated with co-trimoxazole but not on organisms causing infections not usually so treated. Thus the recognition of TMP-resistant pathogens was incomplete.

Screening for asymptomatic carriage of TMP-resistant coliforms—All patients in a particular ward had a rectal swab taken using saline-moistened swabs. These were heavily inoculated without delay on to freshly poured plates of sensitivity test agar (DST, Oxoid) containing

1% lactose, 1% Andrade's indicator, and 10 µg of TMP/ml. Plates were incubated overnight at 37°C, and any coliforms were identified and retested for TMP sensitivity. *Escherichia coli* strains were O-serotyped whenever possible. Patients were classified as carriers when their rectal flora contained any TMP-resistant *E. coli*, *Klebsiella* spp, *Enterobacter* spp, or *Citrobacter* spp.

Determination of minimum inhibitory concentration (MIC)—Pure cultures of coliform organisms were inoculated into 1 ml of Wellcotest broth containing various concentrations of TMP in 75 × 12 mm glass tubes, using an inoculum of 200 organisms, and incubated overnight at 37°C. The MIC of TMP was contained in the tube with the lowest concentration showing no turbidity after incubation.

The outbreak

The history of the outbreak fell into three distinct stages: recognition of the problem, investigation of the factors concerned, and attempts at solution.

RECOGNISING THE PROBLEM

The events surrounding the isolation of the original strain of *E. coli* O18 with a plasmid-mediated TMP resistance have been described.⁵ The organism was a urinary pathogen from a patient in ward 7, and a TMP-resistant *E. coli* O18 was also obtained from the faeces of another patient in that geriatric ward. In the summer of 1972 we realised that many coliform pathogens from patients in St Pancras Hospital were TMP resistant. Many of the infections were of the urinary tract (UTI), and most were in patients in the geriatric wards. Whereas most of the earlier TMP-resistant organisms were *E. coli*, gradually *klebsiellas* became predominant. Because of the earlier recognition of a link between clinical infection and asymptomatic carriage in the bowel flora the outbreak was investigated by screening the whole inpatient population of the hospital for rectal carriage of TMP-resistant coliform bacilli. Table I shows the results of that screening (July–August 1972). Some 49 (17.6%) of the 278 patients were found to be carriers, of whom 41 were in the four geriatric wards.

TABLE I—Results of screening inpatients for rectal carriage of TMP-resistant coliform bacilli, 1972–6

Ward	Type	No of carriers/No of patients screened in:							
		July-Aug 1972	Mar 1973	Apr 1973	July 1973	Jan 1974	Aug 1974	Sep 1975	Oct 1976
1	Female surgical	0/18		0/13	1/24	0/5	1/9	0/10	
3	Male surgical	1/22		2/16	1/16	0/6	2/15	2/16	
4	Male medical	1/20		2/15	2/20	7/20	3/23	1/14	
5	Male geriatric	13/26	5/22	6/26	5/24	5/25	7/17	2/24†	0/19
6	Female medical	3/24		6/25	2/20	0/22	0/19	2/16	
7	Female geriatric	15/29	4/29	2/30*	2/28	2/22	0/23	3/23†	1/16
8	Female geriatric	11/26	2/27	2/29*	2/26	6/26	12/27	1/23†	1/19
9	Mixed geriatric	2/21	4/19	2/19	Closed	6/22	6/25	2/19†	1/21
NWM	Male psychiatric	0/20		0/26	0/24	0/16	0/13	0/16	
NWF	Female psychiatric	0/25		0/21	0/19	1/23	0/15	0/17	
Manson	Mixed tropical	2/25		0/24	1/18	0/19	0/12	0/24	
Chamberlain	Mixed tropical	1/22		0/13	0/20	0/20	1/20	0/25	
Total		49/278		22/277	16/239	27/226	32/218	13/227	
Wards 5, 7, 8, 9 (all geriatric)		41/102	15/97	12/94		19/95	25/92	8/89	3/75

*No sulphonamide, ampicillin, or co-trimoxazole in ward 7 from 1 April 1973.

†No sulphonamide, ampicillin, or co-trimoxazole from 1 December 1974.

INVESTIGATION OF CARRIER STATE

We confined this analysis to the occupants of the four geriatric wards (wards 5, 7, 8, and 9) and examined the case notes of 100 of the 102 patients concerned.

Influence of sex of patient—The carrier rate among the men (50%) was not significantly different from that among the women (47.3%).

Influence of age of patient—Significant differences in age were found (table II), older patients of either sex being more likely to be carriers ($P < 0.001$).

Influence of exposure to antimicrobial agents before screening—Table III shows that patients were more likely to be carriers ($P < 0.01$) if they had previously been given an antimicrobial agent. Carriers were at least twice as likely as non-carriers to have received chemotherapy within about six months before screening. Table IV shows that carriers were more likely to have had chemotherapy and also to have had more courses of antimicrobials than non-carriers. Tables V and VI show

TABLE II—Average ages ($\pm$ SD) of geriatric patients of either sex in relation to carrier state

	Carriers		Non-carriers		P value for difference
	No	Age (years)	No	Age (years)	
Men	13	79.3 $\pm$ 9.4	14	73.6 $\pm$ 7.5	≤ 0.001
Women	28	84.6 $\pm$ 8.0	45	79.8 $\pm$ 7.7	≤ 0.001

TABLE III—Relation between latest treatment with any antimicrobial agent and carrier state

Interval before screening (months)	Carriers (n = 41)		Non-carriers (n = 59)		Significance (χ^2)
	No (%) exposed	No not exposed	No (%) exposed	No not exposed	
0-1	15 (36.6)	26	8 (13.6)	51	$P \leq 0.01$
0-3	23 (56.1)	18	15 (25.4)	44	$P \leq 0.01$
0-6	31 (75.6)	10	24 (40.7)	35	$P \leq 0.01$
0-12	34 (82.9)	7	27 (45.8)	32	$P \leq 0.01$
0-12 +	35 (85.4)	6	39 (66.1)	30	$P \leq 0.01$

that the most important drugs were co-trimoxazole, sulphonamides, and ampicillin. A separate analysis showed that in both sexes those patients above the group mean ages (76.3 years for men and 81.6 years for women) were significantly more likely ($P < 0.05$) to have received any chemotherapy or treatment with co-trimoxazole, sulphonamides, or ampicillin within the previous three months than patients below the group mean age. The size of this effect was such as to establish that the fact that older people were more likely to be carriers (table II) was almost but not entirely explicable on the basis of greater antibiotic exposure.

Influence of duration of hospital stay before screening—The average duration of stay in hospital before screening of geriatric patients was 14.9 months in carriers and 8.1 months in non-carriers. A detailed factorial analysis showed that older patients of either sex stayed in hospital longer, received more antimicrobial chemotherapy (and more treatment with co-trimoxazole, sulphonamides, or ampicillin), and were more likely to become carriers of TMP-resistant coliform

bacilli than younger patients. By far the most important of these factors was treatment with co-trimoxazole, sulphonamides, or ampicillin in the previous months, but duration of hospital stay also contributed.

Summary of analysis of factors determining likelihood of developing carrier state—The overriding predisposing factor to rectal carriage of TMP-resistant organisms was previous antimicrobial chemotherapy, particularly with co-trimoxazole, sulphonamides, or ampicillin. The age of the patient and duration of stay in hospital before screening predisposed mainly in so far as they affected exposure to chemotherapy, though duration of stay in hospital also predisposed independently. Presumably the longer a patient stayed in hospital the more likely he was to be in contact with a carrier and the longer such contact would be, so that his chances of becoming a carrier were increased. The sex of the patient was not a predisposing factor, probably because the exposure to antibiotics was similar for men and women.

TABLE IV—Number of courses of chemotherapy before screening in relation to carrier state

Interval before screening (months)	Carriers (n = 41)		Non-carriers (n = 59)	
	Total No of courses	Average No/patient	Total No of courses	Average No/patient
0-1	20	0.5	10	0.2
0-3	37	0.9	23	0.4
0-6	73	1.8	39	0.7
0-12	100	2.4	57	1.0
0-12 +	129	3.1	85	1.4

TABLE V—Number of exposures to co-trimoxazole, sulphonamides, or ampicillin before screening in relation to carrier state

Interval before screening (months)	Carriers (n = 41)		Non-carriers (n = 59)	
	Total No of exposures	Average No/patient	Total No of exposures	Average No/patient
0-1	16	0.4	6	0.1
0-3	32	0.8	18	0.3
0-6	63	1.5	33	0.6
0-12	88	2.1	44	0.7
0-12 +	144	2.8	68	1.2

TABLE VI—Interval between latest treatment with co-trimoxazole, sulphonamides, or ampicillin before screening in relation to carrier state

Interval before screening (months)	Carriers (n = 41)		Non-carriers (n = 59)		Significance of difference
	No (%) treated	No not treated	No (%) treated	No not treated	
0-1	15 (36.6)	28	4 (6.8)	55	P ≤ 0.01
0-3	21 (51.2)	20	9 (15.2)	50	P ≤ 0.01
0-6	27 (65.9)	14	17 (28.8)	42	P ≤ 0.01
0-12	30 (73.2)	11	19 (32.2)	40	P ≤ 0.01
0-12 +	30 (73.2)	11	21 (35.6)	38	P ≤ 0.01

ATTEMPTS AT SOLUTION

By the time this analysis was completed we had satisfied ourselves that the carrier state was practically important. Between July 1972 and February 1974 some 105 patients were found to be carriers. Of these, 38 (36.2%) developed clinical infections recognised as being caused by TMP-resistant coliform organisms; this was certainly an underestimate. While most TMP-resistant infections were minor, all degrees of severity were seen, including two cases of septicaemia, one of which was fatal. The rectal flora of patients who developed infections with TMP-resistant coliforms yielded similar organisms in 88% of cases.

We chose similar geriatric wards (7 and 8) for study. Each housed about 30 patients on the same landing of the hospital. They had common medical but separate nursing staff. It was agreed that in ward 7 co-trimoxazole, sulphonamides, and ampicillin would not be used as from 1 April 1973, while in ward 8 the medical staff would use whatever chemotherapy was thought appropriate. Any patients in ward 7 who needed a restricted drug would be transferred elsewhere (this happened only once). Table I shows the results of screening the inpatients just before the beginning of the experiment (March 1973) and again in April 1973, January 1974, and August 1974. The level of TMP-resistant carriage was similar in wards 7 and 8 at the beginning of this period. After nine months (January 1974), two out of 22 patients in ward 7 and six out of 26 patients in ward 8 were carriers. After 15 months (August 1974) no carriers were detected among 23 patients in ward 7, whereas in ward 8, 12 out of 27 patients were carriers. In parallel with this clearance of TMP-resistant coliforms from the rectal flora of patients in ward 7, no episodes of UTI caused by such organisms occurred between May 1973 and August 1974 in that ward. In contrast, in ward 8, where carriage of TMP-resistant coliforms continued, nine UTIs due to these organisms occurred during the same period.

From 1 December 1974 the antibiotic restrictions in force in ward 7 were extended to all four geriatric wards (5, 7, 8, and 9). By October

1976 (table I) only three carriers remained among 75 patients in the four wards. TMP-resistant coliforms as a cause of infection had virtually disappeared. Thus newly introduced policies restricting antibiotics produced their maximum effect in about nine months. Of 326 resistant strains of *E coli* and *Klebsiella* spp isolated from infections or from the rectal flora between 1970 and the summer of 1973, 278 had an MIC of TMP of 1000 µg or more/ml. Thus 85% of TMP-resistant coliform organisms isolated had the extremely high MIC associated with plasmid-mediated TMP resistance.⁷ Among the TMP-resistant *E coli* isolated from various sources in the hospital during this outbreak 16 different O-serotypes were identified.

Discussion

The importance of geriatric units as a source of outbreaks of hospital infection is not sufficiently appreciated. Many factors probably contribute to such episodes. Commonly such units contain many patients suffering recurrently from episodes of real or fancied infection, particularly of the urinary and respiratory tracts. Consequently much chemotherapy is used, particularly broad-spectrum drugs. Often the beds are too close together. Urinary and faecal incontinence is common, and the nursing load is so heavy that the hard-pressed staff may sometimes be forced to skimp fundamental measures for controlling cross-infection such as handwashing. Probably the most important factor is the overuse of antibiotics. A striking effect of alerting the medical staff to the problem reported here was the considerable reduction achieved in the chemotherapy prescribed without detriment to the wellbeing of the patients. We believe that much more surveillance of infection and antibiotic usage in geriatric units will be important in preventing similar outbreaks in the future.

When an outbreak of this sort occurs careful analysis may give the key to effective remedial action. This is probably best undertaken jointly by the clinicians and laboratory staff. Without such collaboration in the present study the crucial importance of exposure of patients to ampicillin might have been missed. The point was that the organisms carrying the W plasmid mediating TMP resistance were mostly *E coli* strains at the beginning of the outbreak, but gradually strains of *Klebsiella* spp became predominant. Since *Klebsiella*s are inherently resistant to ampicillin, use of the drug will select these organisms, TMP plasmid included. Thus using an apparently irrelevant antibiotic may select for unrelated resistances. Once the team has established the relevant facts resolute, logically selected policies, jointly implemented, may be expected to control the outbreak, as here. It is, of course, necessary to monitor the effectiveness of the policies, and this, too, should be a joint responsibility.

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