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Effect of stay in hospital and oral chemotherapy on the antibiotic sensitivity of bowel coliforms

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SUMMARY

The effects of oral chemotherapy and stay in hospital on the antibiotic resistance patterns of faecal coliform flora were studied. The coliform flora of 64% of 25 patients who were not receiving antibiotics was sensitive to all drugs tested. Hospitalization alone did not affect this proportion. The administration of tetracycline or ampicillin to patients, whether at home or in hospital, significantly increased the percentage of resistant bowel coliforms. Tetracycline showed a significantly greater effect than ampicillin. There was no significant increase in the percentage of patients with resistant flora after treatment with amoxycillin.

INTRODUCTION

The aerobic Gram-negative normal faecal flora is composed of bacterial genera which are all capable of acquiring plasmids carrying genes coding for drug resistance (R factors). This flora therefore is a huge potential reservoir of resistant organisms which may cause infection in other sites. Factors which affect the antibiotic sensitivity of these faecal organisms will therefore be of importance in determining the resistance patterns of subsequent infections caused by Enterobacteriaceae.

Studies on the flora of normal people not in hospital have shown that bacteria carrying R factors (i.e. R+) are present in a variable proportion of individuals (Datta, 1969; Datta *et al.* 1971; Moorhouse, 1969). In domiciliary patients it was shown that after the oral administration of tetracycline there was a significant increase in the antibiotic resistance of the faecal flora, but this effect was not nearly so great after ampicillin or sulphonamide therapy (Datta *et al.* 1971).

This study describes firstly the incidence of antibiotic-resistant bacteria in the bowel of domiciliary patients in the region of Edinburgh, some of whom had received anti-microbial therapy and others who had not. Secondly, it examines the effect on the bowel flora of the oral administration of anti-microbial agents to hospital patients, and thirdly, the effect of stay in hospital alone on the faecal flora.

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METHODS

The survey

Patients studied were those chosen to investigate the use of amoxycillin in pneumonia and chronic bronchitis (Jones *et al.* 1973). They were admitted to the City Hospital, Edinburgh, in 1971. On admission a rectal swab was taken from each patient and a note made of any anti-microbial treatment which the patient was currently being given. These patients were divided into groups according to which drug had been given before admission to hospital. There were 31 patients who had received ampicillin, 27 who had received tetracycline for less than 1 month, 26 who had received tetracycline for more than 1 month and 64 patients who had received no chemotherapy. The specimen taken at the time of admission was considered to reflect the patient's faecal flora outside hospital.

The 64 patients who had received no antibiotics were studied further. They were allocated to one of three treatment groups (see Jones *et al.* 1973): 23 patients were given tetracycline, 21 ampicillin, and 20 amoxycillin, a new semi-synthetic penicillin related to ampicillin (Sutherland, Croydon & Rolinson, 1972).

Another group of 25 patients, admitted to the same wards for conditions other than pneumonia or chronic bronchitis, and who did not receive antibiotics before or after admission, served as controls. The faecal flora of this control group on admission to hospital was compared with that of the 84 patients who had had antibiotics outside hospital and on discharge with that of the 64 patients who had had antibiotics in hospital.

From the latter two groups a portion of the last faecal specimen passed in hospital was also collected.

Bacteriology

Faecal specimens were spread on MacConkey agar plates for single colonies. Ten separate lactose-fermenting colonies were picked, and identified by ability to produce indole, split urea or use citrate as the sole carbon source. These organisms as a group will be referred to in the remainder of this paper as coliforms. The antibiotic sensitivity of each organism was determined. Oxoid DST agar (CM 261) plates containing 4% lysed blood and one of the following drugs – ampicillin 25 μg./ml., streptomycin 15 μg./ml., tetracycline 10 μg./ml., chloramphenicol 25 μg./ml., kanamycin 10 μg./ml., sulphadimidine 100 μg./ml., nalidixic acid 25 μg./ml., trimethoprim 2 μg./ml. and gentamicin 8 μg./ml. – were inoculated with approximately ten organisms of each strain, using a multiple inoculator, and incubated overnight. A known sensitive and resistant organism were included on each plate. The predominant faecal flora was considered sensitive if all ten colonies picked were sensitive to all the drugs tested. The flora was considered predominantly resistant if five or more of the colonies picked were resistant to at least one of the antibiotics tested. An organism resistant to at least three of the drugs tested was recorded as multi-resistant.

Table 1. *Effect of oral chemotherapy on bowel flora of patients living in the general community*

Antibiotic therapy	No. of patients (10 strains from each patient)	No. of patients with: Sensitive flora (0/10 strains resistant)	No. of patients with: Majority of flora resistant (at least 5/10 strains resistant to at least 1 drug)
None	25	16 (64)	6 (24)
Ampicillin	31	9 (29)	15 (48)
Tetracycline for less than 1 month	27	8 (29)	16 (59)
Tetracycline for more than 1 month	26	2 (8)	22 (84)

Figures in parentheses is percentage of patients.

Table 2. *Antibiograms of multi-resistant organisms obtained from patients in the general community*

Resistance pattern	No. of strains antibiotic therapy: Long-term tetracycline	Short-term tetracycline	Ampicillin
AST	20	—	—
ATC	10	—	—
ASSu	2	—	10
ATSu	1	2	—
STSu	8	10	1
TCSu	—	2	—
ASTSu	11	—	27
ATKSu	—	2	—
STCSu	—	18	—
STKSu	—	2	—
ATCSu	—	1	—
ATCKSu	—	1	—
ASTKSu	—	5	—
ASTCSu	1	19	7
ASTCKSu	1	12	—
Total	54	74	45

A, Ampicillin; S, streptomycin; T, tetracycline; C, chloramphenicol; K, kanamycin; Su, sulphonamide.

RESULTS

Table 1 shows the effect of administration of antibiotics on the faecal flora of 109 patients living in the general community. Of the 25 patients studied who were not receiving antibiotics, 64% had a sensitive flora (i.e. all 10 strains examined were sensitive to all drugs tested), 6 showed a predominantly resistant flora (at least 5/10 strains resistant) and no multi-resistant strains were isolated. The flora of patients who were on antibiotics before admission showed significant differences from those not receiving antibiotics. Only 29% of ampicillin-treated patients had a sensitive flora (difference from untreated group is significant, $P < 0{\cdot}025$). Of 27

Table 3. *Effect of hospitalization and oral chemotherapy on bowel flora of 89 patients admitted to City Hospital, Edinburgh*

Antibiotic given in hospital	No. of patients (10 strains from each patient)		No. of patients with: Sensitive flora (0/10 strains resistant)	No. of patients with: Majority of flora resistant (at least 5/10 strains resistant to at least 1 drug)
—	25	On admission	16 (64)	6 (24)
		On discharge	16 (64)	6 (24)
Tetracycline	23	On admission	9 (39)	10 (43)
		On discharge	1 (4)	22 (96)
Ampicillin	21	On admission	11 (52)	6 (29)
		On discharge	6 (29)	8 (38)
Amoxycillin	20	On admission	8 (40)	7 (35)
		On discharge	6 (30)	10 (50)

Figures in parentheses are percentage of number of patients.

patients treated with tetracycline for less than 4 weeks, 8 had sensitive flora ($P < 0{\cdot}05$) and of the 26 patients who had received tetracycline for a longer period, only 2 had sensitive flora ($P < 0{\cdot}001$). There was no statistical difference in the effect of ampicillin compared with tetracycline on the proportion of patients with sensitive flora (Table 1, column 3). However, tetracycline, whether given for a long or short time, significantly increased the likelihood of the majority of the flora being resistant compared with the untreated groups ($P < 0{\cdot}025$ if treated for less than one month and $P < 0{\cdot}001$ if long-term therapy used) (Table 1, column 4). Ampicillin did not show this effect.

There was a variety of resistance patterns amongst those strains resistant to three or more antibiotics and the patterns are shown in Table 2. There were no organisms found resistant to gentamicin, trimethoprim or nalidixic acid. There was no evidence of a particular antibiotic selecting a particular pattern. However, considering organisms resistant to only one or two antibiotics, there was a much higher incidence of excretion of tetracycline-resistant organisms in those patients receiving tetracycline than of ampicillin resistance in those receiving ampicillin.

Table 3 shows the effect of antibiotics on patients admitted to the City Hospital who had previously not received antibiotic therapy. There were 89 patients studied. Using the chi-square test there is no statistical significance between these groups of patients with respect to having sensitive flora on admission. Of the group who received no chemotherapy, there was no change at the time of discharge in the number of patients with sensitive flora. However, of patients treated with tetracycline there is a highly significant ($P < 0{\cdot}001$) decrease in the number with a sensitive flora and an increase in the number with the majority of the faecal flora antibiotic resistant ($P < 0{\cdot}001$). Ampicillin alters the faecal flora in the same way only to a lesser extent than tetracycline ($P < 0{\cdot}01$). In this series there was no

Table 4. *Duration of stay in hospital*

	Chemotherapy			
	None	Amoxycillin	Tetracycline	Ampicillin
No. of patients	25	20	23	21
Average stay (days)	14·2	16·5	12·3	12·1
Median stay (days)	13	15	13	12

statistically significant decrease in the number of patients whose faecal flora was still sensitive after chemotherapy with amoxycillin. The resistance patterns of the resistant organisms were similar to those occurring in patients prior to admission to hospital. There were no organisms isolated which were resistant to gentamicin, trimethoprim or nalidixic acid.

DISCUSSION

The carriage of R+ coliforms in faecal flora of normal people has been well established but the percentage of resistant organisms has varied enormously in different studies. Datta (1969) found that 52% of 100 patients from the London area who had not received chemotherapy within the previous 6 months, nor been in hospital, carried R+ bacteria, whereas Moorhouse (1969) found the much higher incidence of 81% among Irish infants (but some of these had had previous chemotherapy). In this study we found that in the Edinburgh region 36% of people not receiving antibiotics carried resistant coliforms in the faecal flora and in only one-quarter were they the predominant flora. Multi-resistance was very rare in people not receiving chemotherapy. Admission to hospital alone did not significantly alter the proportion of patients with resistant flora nor the resistance patterns of the coliform population of the bowel. (The average duration of stay in hospital was similar for all groups: see Table 4.) However, chemotherapy significantly changed the bowel flora whether the patient was in hospital or not. Tetracycline caused the greatest change. Ampicillin produced a similar but smaller change but with amoxycillin no change was demonstrated.

The origin of these resistant strains is of interest. It is possible that they are part of the minority flora before therapy and that appropriate drugs inhibit the sensitive flora allowing over-growth of minority strains. This point needs further elucidation.

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