

to use for his own reasons as well as the wider ones of the project of the moment.

Ledgers (whether loose-leaf or not) are probably out of date.

Acknowledgements

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THERAPEUTIC TRIAL

A comparison of the erythromycin estolate and tetracycline in the treatment of respiratory tract infections

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PATIENTS WITH ACUTE EXACERBATIONS OF chronic bronchitis require effective antibiotic therapy for the prompt control of infection. As the range of available antibiotics increases, the selection of the most suitable one for a particular patient becomes more difficult.

Previous trials, in which efficacy of penicillin and tetracycline were compared, failed to demonstrate any significant difference between them (Medical Research Council 1966).

The commonest micro-organism to be encountered in the sputum of patients suffering from acute exacerbations of chronic bronchitis is *Haemophilus influenzae*, which is generally resistant to penicillin. Pneumococci have also been found in proportions varying from 9 to 22 per cent of cases, many of these becoming resistant to tetracycline during or after a course of treatment. (Percival, Armstrong and Turner 1969).

This trial was undertaken to study the effects of erythromycin estolate and tetracycline in the treatment of such cases, and to compare the efficacy of these antibiotics.

Material and Methods

Selection of patients. One hundred patients were initially admitted to the trial, over a period of 18 months. They comprised 72 men between the ages of 48 and 78, and 28 women between the ages of 55 and 85. All the patients were suffering acute exacerbations of chronic bronchitis, and in addition there were in most cases concomitant conditions such as anaemia, congestive cardiac failure, cerebral vascular disease, or senility.

Criteria for admission to the trial were the presence of clinical and radiological evidence of pneumonia, and of purulent sputum. The latter sign was taken as indicative of active

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bacterial infection. The body temperature was measured, but not accepted as the sole criterion of the presence of infection, as it can be an unreliable sign in the elderly.

Laboratory investigations. Fresh sputum specimens were cultured, and antibiotic sensitivities determined at the outset in each case, and usually at the conclusion of treatment also. In 22 cases, a second sputum specimen was not obtainable and progress had to be assessed on clinical and radiological evidence alone. Throat swabs and faecal specimens were examined for the presence of *Candida albicans*.

The following investigations were carried out in those patients treated with erythromycin estolate:

Total white cell count
Haemoglobin
Erythrocyte sedimentation rate
SGOT—estimated by the 'Transac' (Warner) colorimetric method before and after treatment
(Normal values 5-35 units)
SGPT—estimated by the colorimetric method of Reitman and Frankel before and after treatment
(Normal values 5-30 units)

Treatment. Patients were assigned at random to one of the two treatment schedules:

- (1) Erythromycin estolate 250 mg every 6 hours
- (2) Tetracycline 250 mg every 6 hours

This course of treatment was maintained for one week.

Those patients receiving either course of therapy, in whom there was no sign of response after 48 hours, were transferred either to treatment with the other antibiotic under investigation, or else to an entirely different antibiotic. In the latter event the patient took no further part in the trial. Symptomatic therapy, and appropriate treatment for concomitant disease, was prescribed where indicated.

Results

The patients were treated initially as shown in table I.

TABLE I

	<i>Erythromycin estolate</i>	<i>Tetracycline</i>
Men	32 (age 51-78)	40 (age 48-72)
Women	18 (age 61-85)	10 (age 44-83)
<i>Total</i>	50	50

Micro-organisms cultured from the sputum were as follows:

Normal bacterial flora	20 (number of patients)		
<i>H. influenzae</i>	18	''	''
Pneumococcus sp.	22	''	''
Mixed organisms (<i>Staphylococcus aureus</i> , <i>Escherichia coli</i> , and other commensals)	40	''	''

Throat swabs and faecal samples from patients in each group were cultured on Sabouraud's medium and examined before and after treatment for *C. albicans* (table II).

TABLE II

		<i>Erythromycin estolate</i>	<i>Tetracycline</i>
Pre-treatment	Throat	18 +ve	16 +ve
	Stool	6 +ve	7 +ve
Post treatment	Throat	20 +ve	18 +ve
	Stool	6 +ve	12 +ve

*Response to treatment.**Erythromycin estolate*

42 patients responded within 48 hours. Sputum decreased in volume and changed from purulent to mucoid in character by the end of the week's treatment.

Four patients died.

Four patients showed no response to erythromycin estolate after 48 hours and were transferred to treatment with tetracycline.

In three patients, the SGOT was raised (to 80, 65, and 52 units respectively) with serum bilirubin levels of 2mg, 1.8 mg, and 2.5 mg per 100 ml respectively. All returned to normal on cessation of treatment. (The patient with SGOT of 80 units was also suffering from dystrophia myotonica.)

Tetracycline

30 patients responded within 48 hours.

Six patients died.

Eight patients showed no response to tetracycline after 48 hours and were transferred to treatment with erythromycin, to which they showed a good response.

Six patients showed no response to tetracycline after 48 hours and were transferred to treatment with penicillin and streptomycin.

Side effects.

The following side effects were observed:

<i>Erythromycin estolate</i>		<i>Tetracycline</i>	
Abdominal discomfort	2	Nausea and vomiting	4
Difficulty in swallowing	1	Diarrhoea	2*

*In these patients the effect was severe enough for treatment to be discontinued.

Discussion

The majority of patients admitted to hospital with acute exacerbations of chronic bronchitis are admitted after treatment by the family doctor has failed. The prior administration of antibiotics is bound to modify the flora in the sputum, and in some cases may lead to a predominance of resistant strains by the time a patient is admitted to hospital. Difficulty may thus arise in identifying the primary pathogen. Slight predominance in faecal excretion of *C. albicans* following tetracycline therapy has been noted previously (Tewari and Fletcher 1966). On the other hand, the frequency of *C. albicans* in faeces of normal subjects increases with advancing age (Schnoor 1939).

In view of suggestions that erythromycin estolate is capable of provoking liver damage, SGOT estimations were carried out in the patients treated with this antibiotic. Elevated levels were found in only three cases, but the fact that these levels returned to normal on cessation of treatment suggests a causal relationship. It is noteworthy that with some techniques for estimating SGOT, false elevations may be obtained (Sabath, Gerstein and Finland 1968).

Opinions vary on the efficacy of long-term prophylactic use of antibiotics. It is felt that there is a greater likelihood of resistant strains of pathogenic micro-organisms being produced by the use of long-term prophylaxis, and that prompt use of antibiotic therapy at the onset of an acute exacerbation is probably more effective in controlling infection, and at the same time less likely to create resistance.

It remains to be seen whether repeated use of erythromycin estolate would reduce the incidence of re-infection or relapse in chronic bronchitis.

Conclusions

On the basis of the results obtained in this fairly small series of patients, both erythromycin estolate and tetracycline are effective antibiotics for controlling acute exacerbations of chronic bronchitis. Of the two, erythromycin estolate appears to be somewhat more effective.

Summary

One hundred patients with acute exacerbations of chronic bronchitis were given antibiotic therapy with either erythromycin estolate or tetracycline, for seven days. Both antibiotics were found to be

effective in controlling infection in these circumstances. Erythromycin estolate appeared somewhat more effective. Side effects were minimal with both antibiotics.

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