

## A COMPARISON BETWEEN DOXYCYCLINE AND AMPICILLIN IN THE TREATMENT OF BRONCHOPNEUMONIA COMPLICATING MEASLES\*

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### SUMMARY

Fifty-nine cases of measles with bronchopneumonia as a complication were treated with either doxycycline or ampicillin. The differences in the duration of pyrexia and consolidation are discussed and various conclusions drawn. The results did not correspond with sensitivity tests conducted on swabs taken on admission.

Upper respiratory tract infection complicating measles constitutes a major cause of morbidity and mortality. This is particularly hazardous in the Bantu because of their poor resistance caused by undernourishment and other socio-economic conditions.

It is accepted that the commonest offending organisms are staphylococci and streptococci which are sensitive to both tetracycline and penicillin. Jacobs and Robinson<sup>1</sup> evaluated their experiences with doxycycline (Vibramycin)<sup>†</sup> in the acute respiratory infection with favourable results. Aitchison *et al.*<sup>2</sup> had equally good results in chronic bronchitis and De Buse *et al.*<sup>3</sup> after studying and comparing the effects of doxycycline and nonsynthetic penicillin in the outpatient treatment of children with measles complicated by bronchopneumonia, concluded that both drugs were effective.

Examination of numerous laboratory reports from the Infectious Disease Ward of Empilweni Hospital on cultures of nose and throat swabs taken from infants and children suffering from measles and bronchopneumonia established *Staphylococcus pyogenes* as the commonest offending organism.

In this trial, the effectiveness and usefulness of a relatively new tetracycline—doxycycline—is compared with a semisynthetic penicillin—ampicillin—in the treatment of bronchopneumonia complicating measles caused particularly by *Staphylococcus pyogenes*.

### MATERIAL AND METHODS

Fifty-nine patients who were admitted to the Fever Ward of Empilweni Hospital for Bantu suffering from measles complicated by bronchopneumonia were the subjects of this study. Chest X-rays were taken immediately before or on admission and were repeated at weekly intervals until resolution was complete and the patient fit for discharge.

Nose and throat swabs were cultured in order to assess the type of organisms present. Only those cases in which staphylococci were cultured were included in the trial. Each patient was weighed on admission, treatment commenced with either doxycycline or ampicillin in random fashion and temperatures recorded 4-hourly until normal.

The severity of the illness was gauged by the extent of X-ray changes, and classified into mild, moderate and severe groups according to whether 1 or more lobes of the lungs were affected.

Culture and sensitivity reports were received on or about the 5th day of treatment. *In vitro* sensitivities could not be

obtained specifically for doxycycline which was classified as a tetracycline by the laboratory concerned. It should be mentioned that many laboratories put up tetracycline and doxycycline separately because of the variance in spectrum.

TABLE I. COMPARATIVE SENSITIVITY TESTS ON *Staphylococcus pyogenes*

	Ampicillin	Tetracycline
Sensitive .. .. .	42	36
Resistant .. .. .	16	22
Sensitive to both .. .. .		22

Doxycycline was administered orally in a dose of 4 mg/kg body weight/day on admission and thereafter 2 mg/kg/day. Ampicillin was administered in a dose of 125 mg 6-hourly. Both drugs were given for a period of 10 days after which the patient's condition was assessed both clinically and radiologically.

### Patients

Of the 59 patients included in this trial, 31 were treated with doxycycline and 28 with ampicillin.

TABLE II. SEX DISTRIBUTION

	Male	Female
Doxycycline .. .. .	19	12
Ampicillin .. .. .	19	9

TABLE III. AGE DISTRIBUTION

Age	Doxycycline	Ampicillin
0 - 6 months .. .. .	3	1
7 - 12 months .. .. .	13	4
13 - 24 months .. .. .	10	16
25 - 36 months .. .. .	4	3
37 months and over .. .. .	1	4

The severity of the illness on admission and drug distribution are given in Table IV.

TABLE IV. SEVERITY OF ILLNESS AND DRUG DISTRIBUTION

	Mild	Moderate	Severe
Doxycycline .. .. .	6	11	14
Ampicillin .. .. .	4	7	17

In this series 8 deaths were recorded, all having occurred between the 2nd and 12th day of admission. Of these, 5 patients had been treated with doxycycline, 4 cases developing additional complications in the form of congestive cardiac failure and/or gastro enteritis. Of the 3 patients who died in the ampicillin series, all had developed gastro-enteritis and/or congestive cardiac failure as additional complications.

From Table V it is clear that the mortality was related to malnutrition. Using Gomez criteria it is established that the 8 children were also admitted with varying degrees of malnutrition and it would be fair to conclude from the Table, that they had little chance of survival, irrespective of whether they were treated with ampicillin or doxycycline.

\*Date received: 1 February 1971.

†Pfizer Laboratories, Johannesburg.

TABLE V. DEGREE OF MALNUTRITION PER COMEZ CRITERIA, RELATED TO MORTALITY

Age in months	Sex	Weight in kg	Expected weight for age	% of expected weight for age	Degree	Antibiotic
10	M	6.6	9.5	69	2	Doxycycline
9	M	4.3	9.2	48	3	Doxycycline
15	M	7.6	13.8	54	3	Doxycycline
48	M	9.0	16.1	55	3	Ampicillin
6	F	6.3	7.6	83	1	Doxycycline
12	M	7.0	9.8	74	2	Doxycycline
18	F	8.4	9.4	79	1	Ampicillin
11	F	7.4	9.2	81	1	Ampicillin

On comparing the duration of pyrexia and consolidation of the two groups the following results were obtained:

TABLE VI. AVERAGE DURATION IN DAYS

	Doxycycline	Ampicillin
Duration of pyrexia .. ..	5.5	7.3
Duration of consolidation ..	16.4	21.3

## DISCUSSION

De Buse *et al.*<sup>3</sup> comparing the usefulness of doxycycline with nonsynthetic penicillin in outpatient children suffering from measles and bronchopneumonia found no major difference between the two groups.

Fabre *et al.*<sup>4</sup> found that the effective concentration of doxycycline in the body persisted much longer than the other tetracyclines. This is in keeping with the findings of Jacobs and Robinson.<sup>1</sup> Barrettini<sup>5</sup> comparing tonsillar tissue levels between doxycycline and ampicillin showed levels of 1.56 - 4.30 mg/g in the former after 24 hours while no levels were detected with ampicillin.

From this trial, an attempt is made to evaluate the clinical response to the 2 antibiotics by comparing the duration of pyrexia and consolidation in the 2 groups. When considering the X-ray findings one must allow for the fact that the viral process of measles can be the cause of a large part of the X-ray findings which is usually interpreted as bronchopneumonia, as assessed by Kahn and Koiransky.<sup>6</sup>

Although a double-blind trial was not conducted, it is significant that there is a difference of an average of 5 days in the duration of the respiratory consolidation which, in fact, resulted in a shorter stay in hospital for those patients treated with doxycycline. No side-effects were encountered in either group.

Of the 8 deaths in this series, 4 of the 5 patients treated with doxycycline were admitted in congestive cardiac failure and 3 of these were further complicated with gastro-enteritis. The 5th patient had been ill 14 days before admission. Of the 3 patients treated with ampicillin, 2 were admitted in congestive cardiac failure and gastro-enteritis and one with gastro-enteritis only.

Doxycycline is therefore as effective as ampicillin in treating bronchopneumonia complicating measles. Furthermore, the fact that it may be given once daily may be an advantage over penicillin. From Table I and its final result in Table VI, it is possible to assume that the organisms were more sensitive to doxycycline than tetracycline as a whole; and furthermore, that unless sensitivity tests are conducted for doxycycline independently of tetracycline they are of little value.

Penicillins are often preferred to tetracyclines because staining of teeth does not occur. This appears to be less common with doxycyclines than with other tetracyclines due to the reduced calcium bindings and low dosage.

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